Lab to Label:
2025 New Drug Update

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Disclosures

- Given the nature of the presentation, I will include brand names for reference
- Except where noted, information is based upon FDA-approved product labeling

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Objectives

- Identify medications that were approved and came to market in the last year
- Develop a general understanding of each medication's indication, dosing, potential adverse effects, place in therapy, and unique characteristics
- Implement new clinical treatment guidelines that were published in the last year

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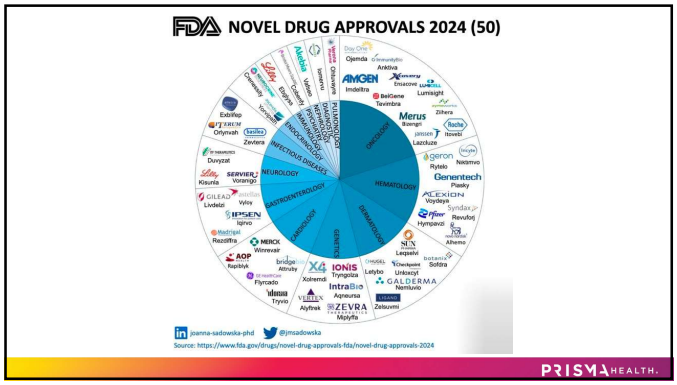

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Outline

- Cardio-Renal-Metabolic
- Infectious Diseases
- Neurology/Psychiatry
- Miscellaneous
- Expanded Access

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Cardio-Renal-Metabolic

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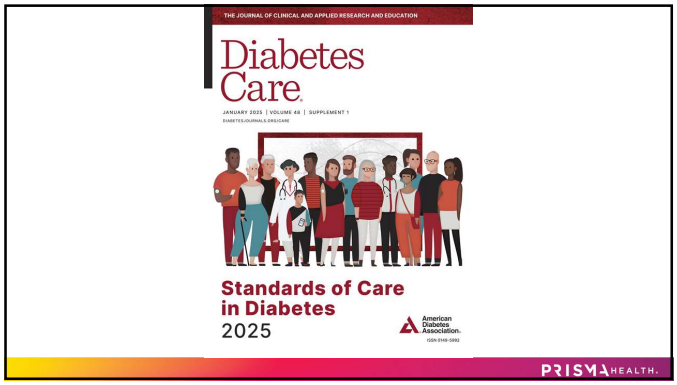

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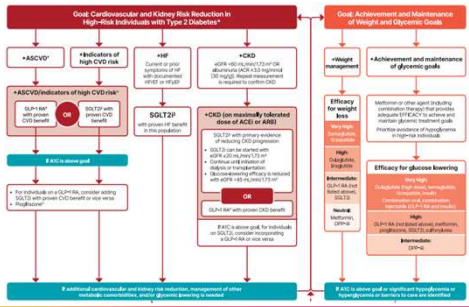
2025 ADA Guideline Recommendations



Diabetes Care 2025;48(Suppl. 1).

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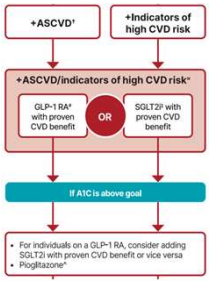
2025 ADA Guideline Recommendations

Goal: Cardiorenal risk reduction

Continues to be independent of glycemic control/A1C goal and concomitant therapies



High risk indicators: Patients ≥55 years old with ≥2: obesity, hypertension, smoking, dyslipidemia, or albuminuria

GLP-1 RA

Dulaglutide (Trulicity)
Liraglutide (Victoza)
Semaglutide (Ozempic)

SGLT2i

Canagliflozin (Invokana)
Empagliflozin (Jardiance)

Diabetes Care 2025;48(Suppl. 1).

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2025 ADA Guideline Recommendations

Goal:
Cardiorenal risk reduction

Heart failure with reduced ejection fraction (HFrEF)
or
heart failure with preserved ejection fraction (HFpEF)

+HF
Current or prior symptoms of HF with documented HFrEF or HFpEF

↓

SGLT2i‡
with proven HF benefit in this population

SGLT2i

Canagliflozin (Invokana)
Dapagliflozin (Farxiga)
Empagliflozin (Jardiance)
Ertugliflozin (Steglatro)

Diabetes Care 2025;48(Suppl. 1).

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2025 ADA Guideline Recommendations

Goal:
Cardiorenal risk reduction

eGFR cut-off for SGLT2i initiation ≥20 mL/min/1.73m²

Labeling varies

Glycemic benefit reduced <30 mL/min/1.73m²

+CKD
eGFR <60 mL/min/1.73 m² OR albuminuria (ACR ≥3.0 mg/mmol [30 mg/g]). Repeat measurement is required to confirm CKD

↓

+CKD (on maximally tolerated dose of ACEi or ARB)

SGLT2i‡ with primary evidence of reducing CKD progression
- SGLT2i can be started with eGFR ≥20 mL/min/1.73 m²
- Continue until initiation of dialysis or transplantation
- Glucose-lowering efficacy is reduced with eGFR <45 mL/min/1.73 m²

OR

GLP-1 RA* with proven CKD benefit

If A1C is above goal, for individuals on SGLT2i, consider incorporating a GLP-1 RA or vice versa

SGLT2i

Canagliflozin (Invokana)
Dapagliflozin (Farxiga)
Empagliflozin (Jardiance)

GLP-1 RA

Dulaglutide (Trulicity)
Liraglutide (Victoza)
Semaglutide (Ozempic)

Also have benefit for renal endpoints in CVOTs

Diabetes Care 2025;48(Suppl. 1).

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2025 ADA Guideline Recommendations

Goal:
Achieve and maintain glycemic and weight management goals

Metformin no longer seems to be a given across the board (2023)

Therapies graded out based upon efficacy towards both glycemic control and weight loss (2023)

+Weight management

Efficacy for weight loss
- Very high: Semaglutide, tirzepatide
- High: Dulaglutide, liraglutide
- Intermediate: GLP-1 RA (not listed above), SGLT2i
- Neutral: Metformin, DPP-4i

+Achievement and maintenance of glycemic goals

Metformin or other agent (including combination therapy) that provides adequate EFFICACY to achieve and maintain glycemic treatment goals

Prioritize avoidance of hypoglycemia in high-risk individuals

Efficacy for glucose lowering
- Very high: Dulaglutide (high dose), semaglutide, tirzepatide, insulin; Combination oral, combination injectable (GLP-1 RA and insulin)
- High: GLP-1 RA (not listed above), metformin, pioglitazone, SGLT2i, sulfonylurea
- Intermediate: DPP-4i

Prioritize avoidance of hypoglycemia in high-risk individuals (2024)

Diabetes Care 2025;48(Suppl. 1).

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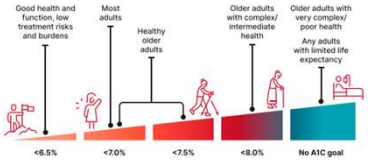
2025 ADA Guideline Recommendations



Modifying Factors

Favor more stringent goal	Favor less stringent goal
Short diabetes duration	Long diabetes duration
Low hypoglycemia risk	High hypoglycemia risk
Low treatment risks and burdens	High treatment risks and burdens
Pharmacotherapy with cardiovascular, kidney, weight, or other benefits	Pharmacotherapy without nonglycemic benefits
No cardiovascular complications	Established cardiovascular complications
Few or minor comorbidities	Severe, life-limiting comorbidities

Diabetes Care 2025;48(Suppl. 1).

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CLINICAL PRACTICE GUIDELINES

2024 ACC/AHA/AACVPR/APMA/ABC/SCAI/SVM/SVN/SVS/SIR/VESS Guideline for the Management of Lower Extremity Peripheral Artery Disease: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines

Circulation.2024;149:e1313-e1410

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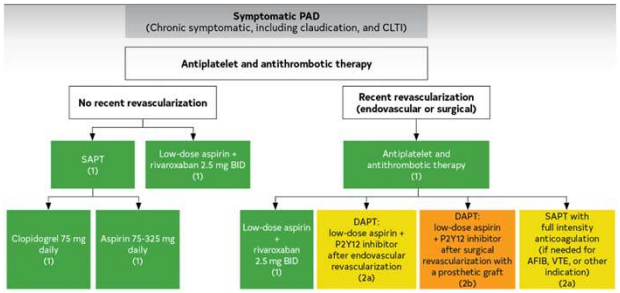
2024 PAD Guideline Recommendations



Circulation.2024;149:e1313-e1410

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CLINICAL PRACTICE GUIDELINES

2024 AHA/ACC/ACS/ASNC/HRS/SCA/SCCT/SCMR/SVM Guideline for Perioperative Cardiovascular Management for Noncardiac Surgery: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines

Circulation.2024;150:e351-e442

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2024 AHA Perioperative Management Recommendations

Preoperative DOAC Schedule

	Procedure Bleeding Risk	Preoperative Interruption						Surgery/ Procedure	Postoperative Resumption			
		Day -6	Day -5	Day -4	Day -3	Day -2	Day -1	Day 0	Day +1	Day +2	Day +3	Day +4
Apixaban, edoxaban, rivaroxaban	High	*	*	*	*	†	†	†	†	†	*	*
	Low/Moderate	*	*	*	*	*	†	†	*	*	*	*
	Minimal	*	*	*	*	*	*	*	*	*	*	*
Apixaban, edoxaban, rivaroxaban with renal impairment (CrCl <30 mL/min)	High	*	*	*	†	†	†	†	†	†	*	*
	Low/Moderate	*	*	*	*	†	†	†	*	*	*	*
	Minimal	*	*	*	*	*	*	*	*	*	*	*
Dabigatran CrCl ≥50 mL/min	High	*	*	*	*	†	†	†	†	†	*	*
	Low/Moderate	*	*	*	*	*	†	†	*	*	*	*
	Minimal	*	*	*	*	*	*	*	*	*	*	*
Dabigatran CrCl <50 mL/min	High	*	*	†	†	†	†	†	†	†	*	*
	Low/Moderate	*	*	*	*	†	†	†	*	*	*	*
	Minimal	*	*	*	*	*	*	*	*	*	*	*

* Do not Hold † Hold DOAC/VKA ‡ Hold and bridge with enoxaparin

Circulation.2024;150:e351-e442

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2024 AHA Perioperative Management Recommendations

VKA Schedule

	Procedure Bleeding Risk	Preoperative Interruption						Surgery/ Procedure	Postoperative Resumption			
		Day -6	Day -5	Day -4	Day -3	Day -2	Day -1	Day 0	Day +1	Day +2	Day +3	Day +4
Warfarin in low/moderate thrombotic risk	High	*	†	†	†	†	†	†	*	*	*	*
	Low/ Moderate	*	†	†	†	†	†	†	*	*	*	*
	Minimal	*	*	*	*	*	*	*	*	*	*	*
Warfarin in high thrombotic risk	High	*	†	†	‡	‡	‡	†	*	*	*ψ	*ψ
	Low/ Moderate	*	†	†	‡	‡	‡	†	*	*ψ	*ψ	*ψ
	Minimal	*	*	*	*	*	*	*	*	*	*	*

* Do not Hold † Hold DOAC/VKA ‡ Hold and bridge with enoxaparin

Circulation.2024;150:e351-e442

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2024 AHA Perioperative Management Recommendations

Thromboembolic Risk for Common Oral Anticoagulant Indications				
Risk Category	Venous Thromboembolism	Atrial Fibrillation	Mechanical Valve	Other Indications
Low	▪ VTE >12 mo	▪ CHA2DS2-VASc 1-4 (without prior history of stroke)	▪ Bileaflet mechanical AVR without major risk factors for stroke	
Moderate	▪ VTE ≤3-12 mo Recurrent VTE	▪ CHA2DS2-VASc 5-6	▪ Bileaflet mechanical AVR with major risk factors for stroke	▪ Herterozygous factor V Leiden ▪ Prothrombin gene mutation ▪ Active cancer
High	▪ Recent VTE (<1 mo or <3 mo)	▪ CHA2DS2-VASc ≥7 (or 5-6 with recent stroke or TIA) ▪ AF with rheumatic valvular heart disease	▪ Mechanical mitral valve Caged ball or tilting-disk valve ▪ Mechanical heart valve in any position with recent stroke or TIA (<3 mo)	▪ Cardioembolic stroke <3 mo ▪ Active cance with high VTE risk ▪ LV thrombus in past< 3 mo ▪ Severe thrombophilia ▪ APS

Circulation.2024;150:e351-e442

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A-proe-see-TEN-tan
(try-vee-oh)

Aprocitentan (Tryvio™)

Indicated to treat hypertension in combination with other antihypertensives

- Mechanism of action: Blocks endothelin (ET)-1 from binding to ET_A and ET_B
  - Preventing vasoconstriction, hypertrophy, inflammation, and fibrosis

Boxed Warning: Embryo-fetal toxicity

FDA Approval: March 2024

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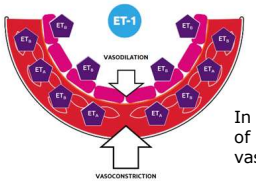
A-proe-see-TEN-tan
(try-vee-oh)

Aprocitentan (Tryvio™)

Indicated to treat hypertension in combination with other antihypertensives



In pathological states, increased expression of ET_B in smooth muscle cells amplifies vasoconstriction effects of endothelin

FDA Approval: March 2024

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Aprocitentan (Tryvio™)

Indicated to treat hypertension in combination with other antihypertensives

- First and only endothelin receptor antagonist for treatment of hypertension
- Once daily dose (12.5 mg tablet)
- If missed dose: skip missed dose and take next regular dose
  - Do NOT take 2 doses in the same day
- Significant drug-drug interactions may impact dose/frequency

Tryvio package insert from Idorsia Pharmaceuticals, revised March 2024

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Aprocitentan (Tryvio™)

PRECISION
(n=730)

Adults with uncontrolled hypertension while on ≥3 antihypertensive medications

1° Endpoints:
Change in mean trough sitting office SBP from baseline to week 4

Overall Demographics

	Apr. 12.5 mg (n=243)	Apr. 25 mg (n=243)	Placebo (n=244)
Age, mean (SD)	61.2 (10.3)	61.7 (10.4)	62.2 (11.2)
Race			
White	203 (84)	200 (82)	202 (83)
Black	28 (12)	28 (12)	26 (11)
Other	12 (5)	15 (6)	16 (6)
Baseline SBP, mmHg	153.2±8.8	153.3±9.0	153.3±9.0
≥4 antiHTN at baselien	151 (62)	158 (65)	151 (62)

Lancet; 2022;S0140-6736.

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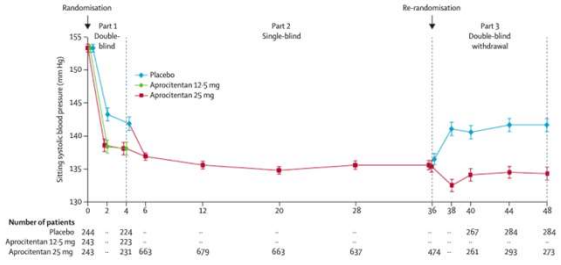
Aprocitentan (Tryvio™)



Lancet; 2022;S0140-6736.

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Aprocitentan (Tryvio™)

Contraindications & Precautions

- Hepatotoxicity
  - Do not start if AST or ALT > 3x ULN
  - Discontinue if signs of hepatic injury
- Fluid retention
  - Do not use in patients with NYHA III or IV HF
- Anemia
  - Not recommended in patient with severe anemia
- Reduced spermatogenesis
- Contraindicated in pregnancy and hypersensitivity

Tryvio package insert from Idorsia Pharmaceuticals, revised March 2024

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Aprocitentan (Tryvio™)

Contraindications & Precautions

- Risk Evaluation and Mitigation Strategy (REMS)
  - Embryo-fetal risk as early as first trimester
  - Patients must have a negative pregnancy test to begin
  - Patients must use adequate birth control
  - Patients should not become pregnant up to 1 month after discontinuation

Boxed Warning: Embryo-fetal toxicity

Tryvio package insert from Idorsia Pharmaceuticals, revised March 2024

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Aprocitentan (Tryvio™)

Pregnancy
- Contraindicated

Lactation
- Not recommended

Pediatric
- Safety and effectiveness not established

Geriatric
- Edema/fluid retention was more common in patients greater than 65 when compared to younger population

Tryvio package insert from Idorsia Pharmaceuticals, revised March 2024

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Aprocitentan (Tryvio™)

Copay Cards

- As low as $10 per month through Walgreens Speciality
- https://www.tryvio.com/#copay

Patient Assistance

- Unknown

Tryvio package insert from Idorsia Pharmaceuticals, revised March 2024

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Landiolol (Rapiblyk™)

lan-di-o-LOL
(rap-ib-lick)

Indicated to treat supraventricular tachycardia

- Mechanism of action: a selective beta-1-adrenoreceptor antagonist
  - inhibits the positive chronotropic effects of the catecholamines, epinephrine and norepinephrine, on the heart

FDA Approval: November 2024

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Landiolol (Rapiblyk™)

Indicated to treat supraventricular tachycardia

Initial	Titration	Max Dose
• 9 mcg/kg/min • 1 mcg/g/min (impaired cardiac function)	• 9 mcg/kg/min q 10 min • 1 mcg/kg/min q 15 min (impaired cardiac function)	• 36 mcg/kg/min

9 mcg/kg/min landiolol is equivalent to 9.6 mcg/kg/min landiolol hydrochloride

Rapiblyk package insert from AOP Health, revised November 2024

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Landiolol (Rapiblyk™)

Landi-SEP
(n=196)

Adults ≥ 18 years old with septic shock with persistent tachycardia (HR≥95 bpm) despite hemodynamic optimization phase of 12-36 hours

1º Endpoints:
Multi-component endpoint of HR-response, HR maintenance, and no increase in vasopressors

Overall Demographics

	Landiolol (n=98)	Placebo (n=98)
Age, mean (SD)	64.4 (12.5)	65.2 (15.06)
SOFA, mean (SD)	12.6 (3.54)	12.1 (2.83)
MAP, mean (SD)	78.6 (10.2)	79 (10.36)
Mech Ventilation	83 (85)	78 (80)
Female	35 (36)	43 (44)
Atrial Fibrillation	26 (27)	24 (24)

Intensive Care Med (2024) 50:1622–1634

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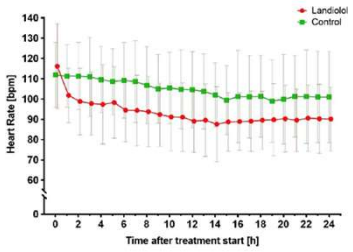
Landiolol (Rapiblyk™)

Landi-SEP
(n=196)

Adults ≥ 18 years old with septic shock with persistent tachycardia (HR≥95 bpm) despite hemodynamic optimization phase of 12-36 hours

1º Endpoints:
Multi-component endpoint of HR-response, HR maintenance, and no increase in vasopressors



Intensive Care Med (2024) 50:1622–1634

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Landiolol (Rapiblyk™)

Contraindications & Precautions

- Severe sinus bradycardia
- Sick sinus syndrome
- Heart block greater than first degree
- Decompensated heart failure
- Cardiogenic shock
- Pulmonary hypertension

Rapiblyk package insert from AOP Health, revised November 2024

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Landiolol (Rapiblyk™)

Contraindications & Precautions

- Adverse Reactions
  - Hypotension

Rapiblyk package insert from AOP Health, revised November 2024

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Landiolol (Rapiblyk™)

Pregnancy
- Insufficient data to evaluate risk for adverse maternal or fetal outcomes

Lactation
- No data on presence in human milk. Not recommended while breast feeding

Pediatric
- Safety and effectiveness not established

Geriatric
- No data available (clinical trials did not include significant number of patients > 65 years)

Rapiblyk package insert from AOP Health, revised November 2024

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Landiolol (Rapiblyk™)

Copay Cards
- Unknow/Not applicable
- Inpatient Medication

Patient Assistance
- Unknow/Not applicable
- Inpatient Medication

Rapiblyk package insert from AOP Health, revised November 2024

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Olezarsen (Tryngolza™)

Ol-es-Ar-sin
(Tren-GOL-zuh)

Indicated to treat familial chylomicronemia syndrome

- Mechanism of action: ASO-GalNAc3 conjugate that binds to apoC-III mRNA leading to mRNA degradation and resulting in a reduction of serum apoC-III protein.
  - Reduction of apoC-III protein leads to increased clearance of plasma TG and VLDL.

FDA Approval: December 2024

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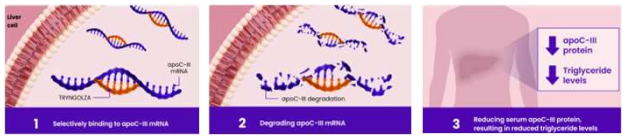
Olezarsen (Tryngolza™)

Indicated to treat familial chylomicronemia syndrome



https://tryngolzahcp.com/about-tryngolza/mechanism-of-action

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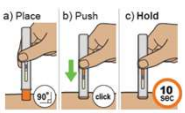
Olezarsen (Tryngolza™)

Indicated to treat familial chylomicronemia syndrome

- Dose: 80 mg subcutaneously once monthly
  - Single dose autoinjector
  - Store in refrigerator, remove from 30 minutes prior to administration
- Maintain a low-fat diet (≤20g fat per day)



Tryngolza package insert from Ionis Pharmaceuticals, revised December 2024

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Olezarsen (Tryngolza™)

Balance Trial
(n=66)

Adults ≥18 years old with familial chylomicronemia syndrome

1° Endpoints:
Percent change in fasting triglycerides levels from baseline to 6 months.

Overall Demographics

	Olezarsen 80 mg (n=22)	Olezarsen 50 mg (n=21)	Placebo (n=23)
Age, mean (SD)	47.7 (13.3)	43.2 (12.1)	44.0 (14.7)
Race			
White	17 (77)	17 (81)	22 (96)
Hispanic	1 (5)	3 (14)	3 (13)
Asian	3 (14)	3 (14)	0 (0)
Female	11 (50)	15 (71)	12 (52)
Triglyceride level, mean (SD)	2613 (1499)	2684 (1235)	2596 (1256)

N Engl J Med 2024;390:1781-92.

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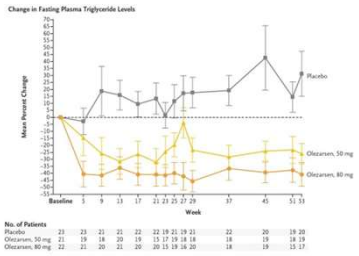
Olezarsen (Tryngolza™)

Balance Trial
(n=66)

Adults ≥18 years old with familial chylomicronemia syndrome

1° Endpoints:
Percent change in fasting triglycerides levels from baseline to 6 months.



N Engl J Med 2024;390:1781-92.

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Olezarsen (Tryngolza™)

Contraindications & Precautions

- Hypersensitivity to olezarsen or any excipient of TRYNGOLZA

Tryngolza package insert from Ionis Pharmaceuticals, revised December 2024

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Olezarsen (Tryngolza™)

Contraindications & Precautions

- Adverse Reactions
  - Injection site reactions
  - Decreased platelet counts
  - Arthralgias

Tryngolza package insert from Ionis Pharmaceuticals, revised December 2024

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Olezarsen (Tryngolza™)

Pregnancy
- Insufficient data to evaluate risk for adverse maternal or fetal outcomes

Lactation
- No data on presence in human milk. Not recommended while breast feeding

Pediatric
- Safety and effectiveness not established

Geriatric
- No overall difference in safety or effectiveness observed in patients greater than 65 when compared to younger population

Tryngolza package insert from Ionis Pharmaceuticals, revised December 2024

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Olezarsen (Tryngolza™)

Copay Cards

- As low as $0 per fill
- https://tryngolza.com/support-and-access/access

Patient Assistance

- Ionis Every Step Support Program
- https://tryngolza.com/support-and-access/access

Tryngolza package insert from Ionis Pharmaceuticals, revised December 2024

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Acoramidis (Attruby™)

a-cor-AM-i-dis
(a-TRUE-bee)

Indicated to treat cardiomyopathy of wild-type or variant transthyretin-mediated amyloidosis

- Mechanism of action: a selective stabilizer of transthyretin (TTR).
  - Binds TTR at thyroxine binding sites and slows dissociation of the TTR tetramer into monomers
    - Rate-limiting step in amyloidogenesis.

FDA Approval: November 2024

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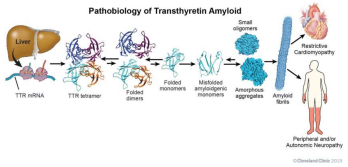
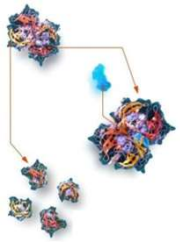
Acoramidis (Attruby™)

a-cor-AM-i-dis
(a-TRUE-bee)





J Am Coll Cardiol. 2019;73 (23):2872–91

FDA Approval: November 2024

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Acoramidis (Attruby™)

Indicated to treat cardiomyopathy of wild-type or variant transthyretin-mediated amyloidosis

- Dose: 712 mg (2 Tablets) orally twice daily (with or without food)
- Do not crush, cut, or chew

Attruby package insert from BridgeBio, revised November 2024

PRISMA HEALTH.

48

Acoramidis (Attruby™)

ATTRibute-CM
(n=632)

Adults 18-90 years with Transthyretin amyloid cardiomyopathy and heart failure (HF) with ≥1 hospitalization for HF, volume overload, or diuretic treatment.

1° Endpoints:
4-step hierarchical analysis of death, CV hospitalization, change in NT-proBNP, and 6-min walk distance

Overall Demographics

		Acoramidis (n=421)	Placebo (n=211)
Age, mean (SD)		77.4 (6.5)	77.1 (6.8)
Race			
	White	368 (87.4)	187 (88.6)
	Black	20 (4.8)	10 (4.7)
	Asian	10 (2.4)	3 (1.4)
Female		37 (8.8)	25 (11.8)
NYHA II		293 (69.6)	162 (76.8)
NYHA III		77 (18.3)	32 (15.2)

N Engl J Med 2024.390;132-142 CV: Cardiovascular; NYHA: New York Heart Association

PRISMA HEALTH.

49

Acoramidis (Attruby™)

ATTRibute-CM
(n=632)

Adults 18-90 years with Transthyretin amyloid cardiomyopathy and heart failure (HF) with ≥1 hospitalization for HF, volume overload, or diuretic treatment.

1° Endpoints:
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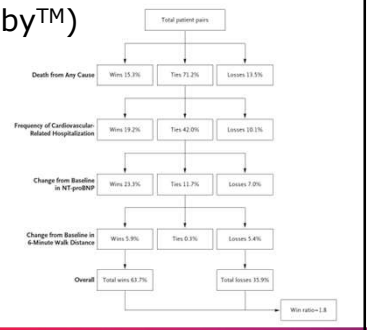


N Engl J Med 2024.390;132-142

PRISMA HEALTH.

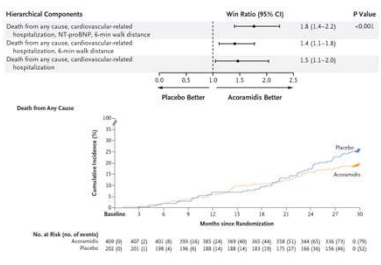
50

Acoramidis (Attruby™)

ATTRibute-CM
(n=632)

Adults 18-90 years with Transthyretin amyloid cardiomyopathy and heart failure (HF) with ≥1 hospitalization for HF, volume overload, or diuretic treatment.

1° Endpoints:
4-step hierarchical analysis of death, CV hospitalization, change in NT-proBNP, and 6-min walk distance



N Engl J Med 2024.390;132-142

PRISMA HEALTH.

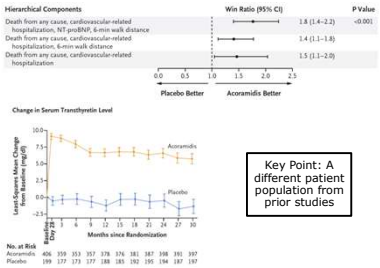
51

Acoramidis (Attruby™)

ATTRibute-CM (n=632)

Adults 18-90 years with Transthyretin amyloid cardiomyopathy and heart failure (HF) with ≥1 hospitalization for HF, volume overload, or diuretic treatment.

1° Endpoints:
4-step hierarchical analysis of death, CV hospitalization, change in NT-proBNP, and 6-min walk distance



Key Point: A different patient population from prior studies

N Engl J Med 2024.390;132-142

PRISMA HEALTH.

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Acoramidis (Attruby™)

Contraindications & Precautions

- No contraindications listed in FDA labeling

Attruby package insert from BridgeBio, revised November 2024

PRISMA HEALTH.

53

Acoramidis (Attruby™)

Contraindications & Precautions

- Adverse Reactions
  - Diarrhea
  - Abdominal pain

Attruby package insert from BridgeBio, revised November 2024

PRISMA HEALTH.

54

Acoramidis (Attruby™)

Pregnancy
- Insufficient data to evaluate risk for adverse maternal or fetal outcomes

Lactation
- No data on presence in human milk. Not recommended while breast feeding

Pediatric
- Safety and effectiveness not established

Geriatric
- No overall difference in safety or effectiveness observed in patients greater than 65 when compared to younger population

Attruby package insert from BridgeBio, revised November 2024

PRISMA HEALTH.

55

Acoramidis (Attruby™)

Copay Cards
- As low as $0 per fill
- https://forgingbridges.com/patient/financial/

Patient Assistance
- Forging Bridges Support
- https://forgingbridges.com/patient/financial/

Attruby package insert from BridgeBio, revised November 2024

PRISMA HEALTH.

56

Sotatercept-csrk (Winrevair™)

Soe-TAT-er-sept
(Win-reh-vare)

Indicated to treat pulmonary arterial hypertension (WHO Group 1)

- Mechanism of action: Binding of serveral endogenous transforming growth factor-beta (TGF-B) superfamily ligands
  - Resulting in a balance between pro-proliferative Act RIIA/Smad2/3 and anti-proliferative BMPRII/Smad 1/5/8 signaling to modulate vascular proliferation

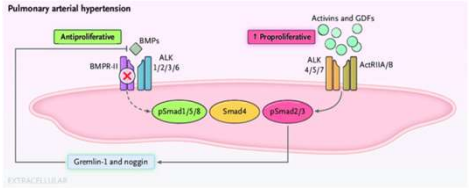
FDA Approval: March 2024

PRISMA HEALTH.

57

Sotatercept-csrk (Winrevair™)

Indicated to treat pulmonary arterial hypertension (WHO Group 1)

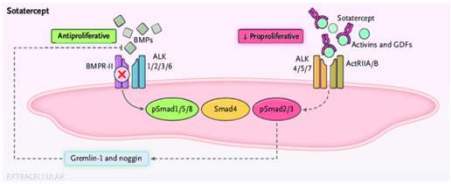


Winrevair package insert from Merck Sharp & Dohme LLC, revised March 2024

58

Sotatercept-csrk (Winrevair™)

Indicated to treat pulmonary arterial hypertension (WHO Group 1)



Winrevair package insert from Merck Sharp & Dohme LLC, revised March 2024

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Sotatercept-csrk (Winrevair™)

Indicated to treat pulmonary arterial hypertension (WHO Group 1)

- Initial dose: 0.3 mg/kg subcutaneously once every 3 weeks
- Increase to target dose 0.7 mg/kg once every 3 weeks once Hb and Plts stabilize in acceptable range
- Missed dose: administer dose as soon as possible
  - If not administered within 3 days of original scheduled: adjust scheduled to maintain every 3-week interval.

Winrevair package insert from Merck Sharp & Dohme LLC, revised March 2024

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Sotatercept-csrk (Winrevair™)

STELLAR
(n=323)

Adults with a confirmed diagnosis of PAH in WHO class II or III

1° Endpoints:
Change in 6-minute walk distance from baseline to week 24

Overall Demographics

	Sotatercept (n=163)	Placebo (n=160)
Age, mean ± SD	47.6±14.1	48.3±15.5
Race		
White	147 (90%)	141 (88%)
Black	2 (1%)	5 (3%)
Other	14 (9%)	14 (9%)
Years since diagnosis	9.2±7.3	8.3±6.7
WHO functional class		
II	79 (49%)	78 (49%)
III	84 (51%)	82 (51%)

NEJM; 2023;388:1478-90

PRISMA HEALTH.

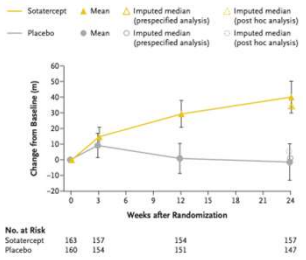
61

Sotatercept-csrk (Winrevair™)

STELLAR
(n=323)

Adults with a confirmed diagnosis of PAH in WHO class II or III

1° Endpoints:
Change in 6-minute walk distance from baseline to week 24



NEJM; 2023;388:1478-90

PRISMA HEALTH.

62

Sotatercept-csrk (Winrevair™)

Contraindications & Precautions

- Erythrocytosis
  - Increased Hb may occur, leading to increase thromboembolic events
  - Hold dose for 3 weeks if: Hb Increase > 2g/dL from previous dose, >4g/dL from baseline or > 2g/dL above ULN
- Thrombocytopenia
  - Reported more frequently in patients receiving prostacyclin infusions
  - Hold dose for 3 weeks if: Plt decrease to < 50,0000 mm^3
- Embryo-fetal toxicity
  - Patients should not become pregnant for up to 4 months after discontinuation

Winrevair package insert from Merck Sharp & Dohme LLC, revised March 2024

PRISMA HEALTH.

63

Sotatercept-csrk (Winrevair™)

Contraindications & Precautions

- Adverse reactions (>10%)
  - Diarrhea
  - Headache, Dizziness
  - Epistaxis
  - Erythema, rash, telangiectasia
  - Antibody development

Winrevair package insert from Merck Sharp & Dohme LLC, revised March 2024

PRISMA HEALTH.

64

Sotatercept-csrk (Winrevair™)

Pregnancy
- Animal studies found fetal harm

Lactation
- Not recommended

Pediatric
- Safety and effectiveness not established

Geriatric
- No overall difference in safety or effectiveness observed in patients greater than 65 when compared to younger population

Winrevair package insert from Merck Sharp & Dohme LLC, revised March 2024

PRISMA HEALTH.

65

Sotatercept-csrk (Winrevair™)

Copay Cards
- As low as $5 per fill
- https://www.merckaccessprogram-winrevair.com/hcp/affordability/

Patient Assistance
- Merck Patient Assistance Program
- https://www.merckaccessprogram-winrevair.com/hcp/affordability/

Winrevair package insert from Merck Sharp & Dohme LLC, revised March 2024

PRISMA HEALTH.

66

Ensifentrine (Ohtuvayre™)

En-sef-in-treen (OH-too-vare)

Indicated as maintenance treatment of chronic obstructive pulmonary disease in adult patients

- Mechanism of action: small molecule that is an inhibitor of PDE3 and PDE4
  - PDE3 primarily hydrolyzes the second-messenger molecule cyclic adenosine monophosphate (cAMP) but is also capable of hydrolyzing cyclic guanosine monophosphate (cGMP)
  - PDE4 hydrolyzes cAMP only. Inhibition of PDE3 and PDE4 results in accumulation of intracellular levels of cAMP and/or cGMP, resulting in various downstream signaling effects.
- Recommended Dosage: 3 mg (one ampule) twice daily administered by oral inhalation using a standard jet nebulizer with a mouthpiece

FDA Approval: June 2024

PRISMA HEALTH.

67

Ensifentrine (Ohtuvayre™)

En-sef-in-treen (OH-too-vare)

Indicated as maintenance treatment of chronic obstructive pulmonary disease in adult patients

Dual Mechanism of action produces:
- Bronchodilation
- Anti-inflammation through decreased inflammatory cell recruitment and infiltration into the lung

FDA Approval: June 2024

PRISMA HEALTH.

68

Ensifentrine (Ohtuvayre™)

ENHANCE-1
(n=760)

Adults aged 40–80 years, with COPD, a post-bronchodilator FEV1 30–70% I, and a smoking history ≥ 10 pack-years

1° Endpoints:
Change in mean FEV_1 $AUC_{0\text{-}12h}$ from baseline to week 12

Overall Demographics

	Ensifentrine (n=477)	Placebo (n=283)
Age, mean ± SD	65.1±7.1	64.9±7.7
Race		
White	435 (91%)	250 (88%)
Black	16 (3%)	9 (3%)
Other	26 (6%)	24 (9%)
Maintenance used	331 (69%)	192 (68%)
Severity		
GOLD 2	294 (62%)	164 (58%)
GOLD 3	179 (38%)	119 (42%)

Am J Respir Crit Care Med 2023;208:406-416

PRISMA HEALTH.

69

Ensifentrine (Ohtuvayre™)

ENHANCE-2
(n=789)

Adults aged 40–80 years, with COPD, a post-bronchodilator FEV1 30–70% I, and a smoking history ≥ 10 pack-years

1° Endpoints:
Change in mean FEV_1 AUC_{0-12h} from baseline to week 12

Overall Demographics			
		Ensifentrine (n=498)	Placebo (n=291)
Age, mean ± SD		65.0±7.4	65.3±7.3
Race			
	White	471 (95%)	276 (95%)
	Black	24 (5%)	11 (5%)
	Other	3 (<1%)	4 (<1%)
Maintenance used		275 (55%)	160 (55%)
Severity			
	GOLD 2	265 (53%)	143 (49%)
	GOLD 3	231 (46%)	148 (51%)

Am J Respir Crit Care Med:2023;208:406-416

PRISMA HEALTH.

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Ensifentrine (Ohtuvayre™)

	ENHANCE-1		ENHANCE-2	
	Ensifentrine	Placebo	Ensifentrine	Placebo
Mean baseline FEV_1, ml (SD)	1420 (487)	1403 (468)	1285 (451)	1279 (473)
Week 12 mean FEV_1 $AUC_{0-12\ h}$ Change from baseline, ml (95% CI)	61 (25, 97)	-26 (-64, 13)	48 (30, 66)	-46 (-70, -22)
Ensifentrine vs. Placebo, ml (95% CI)	87 (55, 119)		94 (65, 124)	
P-value	< 0.001		<0.001	

Am J Respir Crit Care Med:2023;208:406-416

PRISMA HEALTH.

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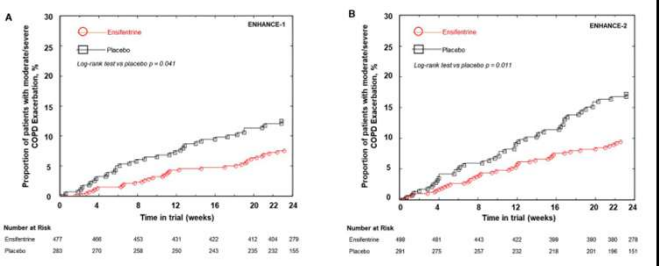
Ensifentrine (Ohtuvayre™)



Am J Respir Crit Care Med:2023;208:406-416

PRISMA HEALTH.

72

Ensifentrine (Ohtuvayre™)

Contraindications & Precautions

- Acute episodes of bronchospasm
  - Do not use to treat acute symptoms of bronchospasm.
- Paradoxical bronchospasm
  - Discontinue and start alternative therapy
- Psychiatric adverse reactions, including suicidality
  - Cautious use with history of depression or suicidal thoughts or behaviors

Ohtuvayre package insert from Verona Pharma, revised June 2024

PRISMA HEALTH.

73

Ensifentrine (Ohtuvayre™)

Pregnancy
- No data available

Lactation
- No data available

Pediatric
- Safety and effectiveness not established

Geriatric
- No overall difference in safety or effectiveness observed in patients greater than 65 when compared to younger population

Ohtuvayre package insert from Verona Pharma, revised June 2024

PRISMA HEALTH.

74

Ensifentrine (Ohtuvayre™)

Copay Cards

- As low as $0 per fill
- Free Trial Available
- https://ohtuvayre.com/cost-assistance/

Patient Assistance

- Verona Pathway Plus
- https://ohtuvayrehcp.com/access-patient-support/

Ohtuvayre package insert from Verona Pharma, revised June 2024

PRISMA HEALTH.

75

VAN-zah-KAF-tor TEZ-a-KAF-tor due-TIV-a-KAF-tor (ah-LIF-trek)

Vanzacaftor, tezacaftor, and deutivacaftor (Alyftrek™)

Indicated to treat cystic fibrosis

- Mechanism of action:
  - **Vanzacaftor** and **tezacaftor** bind to different sites on the CFTR protein and have an additive effect in facilitating the cellular processing and trafficking of select mutant forms of CFTR
  - **Deutivacaftor** potentiates the channel open probability (or gating) of the CFTR protein at the cell surface.

Boxed Warning: Drug-induced liver injury and liver failure

FDA Approval: December 2024

PRISMA HEALTH.

76

Vanzacaftor, tezacaftor, and deutivacaftor (Alyftrek™)

Indicated to treat cystic fibrosis

Recommended Dosage for Adults and Pediatric Patients Aged 6 Years and Older		
Age	Weight	Once Daily Oral Dosage
6 to less than 11 years	< 40 kg	Three tablets of vanzacaftor 4mg/tezacaftor 20 mg/deutivacaftor 50 mg
	≥ 40 kg	Two tablets of vanzacaftor 10 mg/tezacaftor 50 mg/deutivacaftor 125 mg
≥ 12 years old	Any Weight	Two tablets of vanzacaftor 10 mg/tezacaftor 50 mg/deutivacaftor 125 mg

Alyftrek package insert from VERTEX, revised December 2024

PRISMA HEALTH.

77

Vanzacaftor, tezacaftor, and deutivacaftor (Alyftrek™)

Uluer et al. Part 1 (n=58)

Adults ≥ 18 years old with cystic fibrosis with a CFTR gating mutation previously stable on ivacaftor monotherapy

1° Endpoints:
Absolute change in ppFEV1 from baseline to week 12

Baseline Demographics				
	Van 5 mg (n=9)	Van 10 mg (n=19)	Van 20 mg (n=20)	Placebo (n=10)
Age, mean (SD)	33.0 (11.4)	30.8 (9.1)	36.4 (11.7)	30.6 (5.9)
Race				
White	8 (89)	18 (95)	17 (85)	10 (100)
Black	0 (0)	1 (5)	0 (0)	0 (0)
Other	0 (0)	0 (0)	2 (10)	0 (0)
Female	4 (44)	3 (16)	9 (45)	2 (20)
ppFEV1 (% pt)	62.3 (13.2)	58.5 (13.2)	60.1 (13.0)	51.8 (13.1)

Lancet Respir Med 2023; 11: 550–62

PRISMA HEALTH.

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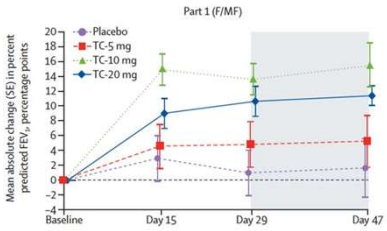
Vanzacaftor, tezacaftor, and deutivacaftor (Alyftrek™)

Uluer et al. Part 1
(n=58)

Adults ≥ 18 years old with cystic fibrosis with a CFTR gating mutation previously stable on ivacaftor monotherapy

1° Endpoints:
Absolute change in ppFEV1 from baseline to week 12



Lancet Respir Med 2023; 11: 550–62

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Vanzacaftor, tezacaftor, and deutivacaftor (Alyftrek™)

Uluer et al. Part 2
(n=28)

Adults ≥ 18 years old with cystic fibrosis with ppFEV1 between 40 and 90 percentage points

1° Endpoints:
Absolute change in ppFEV1 from baseline to day 29

Baseline Demographics

	Tezacaftor-ivacaftor (n=10)	Van 20 mg (n=18)
Age, mean (SD)	33.0 (8.3)	30.8 (8.7)
Race		
White	9 (90)	18 (100)
Black	0 (0)	0 (0)
Other	0 (0)	0 (0)
Female	2 (20)	7 (39)
ppFEV1 (% pt)	57.4 (15.1)	60.9 (15.4)

Lancet Respir Med 2023; 11: 550–62

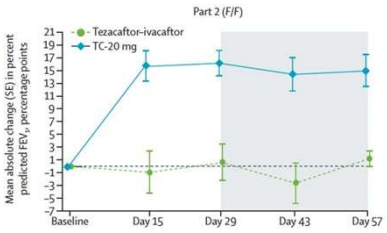
80

Vanzacaftor, tezacaftor, and deutivacaftor (Alyftrek™)

Uluer et al. Part 2
(n=28)

Adults ≥ 18 years old with cystic fibrosis with ppFEV1 between 40 and 90 percentage points

1° Endpoints:
Absolute change in ppFEV1 from baseline to day 29



Lancet Respir Med 2023; 11: 550–62

81

Vanzacaftor, tezacaftor, and deutivacaftor (Alyftrek™)

Contraindications & Precautions

- Hypersensitivity to vanzacaftor, tezacaftor, deutivacaftor or any excipient of ALYFTREK

Alyftrek package insert from VERTEX, revised December 2024

82

Vanzacaftor, tezacaftor, and deutivacaftor (Alyftrek™)

Contraindications & Precautions

- Adverse Reactions
  - Elevated transaminases
  - Cataracts (reported with ivacaftor)
  - Cough
  - Nasopharyngitis
  - Upper respiratory tract infection
  - Headache
  - Fatigue
  - Rash

Alyftrek package insert from VERTEX, revised December 2024

83

Vanzacaftor, tezacaftor, and deutivacaftor (Alyftrek™)

Pregnancy
- Insufficient data to evaluate risk for adverse maternal or fetal outcomes

Lactation
- No data on presence in human milk. Not recommended while breast feeding

Pediatric
- Safety and effectiveness established in patients 6 years or older with at least one F508del mutation or another responsive mutation

Geriatric
- No data available (clinical trials did not include significant number of patients > 65 years)

Alyftrek package insert from VERTEX, revised December 2024

84

Vanzacaftor, tezacaftor, and deutivacaftor (Alyftrek™)

Copay Cards

- As low as $0 per fill
- https://www.vertexgps.com/financial-assistance//www.vertexgps.com/financial-assistance

Patient Assistance

- Unknown

Alyftrek package insert from VERTEX, revised December 2024

PRISMA HEALTH.

85

Vadadustat (Vafseo®)

Vad-a-doo-stat (VAFF-see-oh)

Indicated to treat anemia due to chronic kidney disease in adults who have been receiving dialysis for at least three months.

- Mechanism of action: Reversible inhibitor of HIF-prolyl-4-hydroxylases (PH)1, PH2, and PH3 (IC50 in the nM range).
  - Results in the stabilization and nuclear accumulation of HIF-1α and HIF-2α transcription factors, and increased production of erythropoietin (EPO).

Boxed warning: increased risk of death, myocardial infarction, stroke, venous thromboembolism, and thrombosis of vascular access.

FDA Approval: March 2024

PRISMA HEALTH.

86

Vadadustat (Vafseo®)

Vad-a-doo-stat (VAFF-see-oh)

Indicated to treat anemia due to chronic kidney disease in adults who have been receiving dialysis for at least three months.

FDA Approval: March 2024

PRISMA HEALTH.

87

Vadadustat (Vafseo®)

Indicated to treat anemia due to chronic kidney disease in adults who have been receiving dialysis for at least three months.

- Recommended starting dose is 300 mg orally once daily, with or without food
- Monitor hemoglobin levels when initiating, then monthly
- Increase the dose no more frequently than once every 4 weeks. Decreases in dose can occur more frequently
  - Adjust dose in increments of 150 mg to achieve or maintain hemoglobin levels of 10 g/dL to 11 g/dL.
  - Doses may range from 150 mg to a maximum of 600 mg.

Vafseo package insert from Akebia Therapeutics, revised March 2024

PRISMA HEALTH.

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Vadadustat (Vafseo®)

$INNO_2VATE$-1
(n=369)

Adults with CKD on HD

1° Endpoints:
the first occurrence of an adjudicated major adverse cardiovascular event (MACE) — pooled across the two trials.

Overall Demographics

	Vadadustat (n=181)	Darbepoetin Alfa (n=188)
Age, mean ± SD	56.5±14.8	55.6±14.6
Race		
White	129 (71%)	143 (76)
Black	38 (21%)	35 (19)
Other	14 (8%)	10 (5)
Years since initiation of dialysis	0.14±0.09	0.15±0.28
Type of dialysis		
Hemodialysis	158 (87%)	169 (91%)
Peritoneal dialysis	22 (12%)	16 (9%)
Combination	3 (2%)	1 (1%)

N Engl J Med 2021;384:1601-1612

PRISMA HEALTH.

89

Vadadustat (Vafseo®)

$INNO_2VATE$-2
(n=3554)

Adults with CKD on HD

1° Endpoints:
the first occurrence of an adjudicated major adverse cardiovascular event (MACE) — pooled across the two trials.

Overall Demographics

	Vadadustat (n=1777)	Darbepoetin Alfa (n=1777)
Age, mean ± SD	57.9±13.9	58.4±13.8
Race		
White	1135 (64%)	1096 (62%)
Black	432 (24%)	444 (25%)
Other	210 (12%)	237 (13%)
Years since initiation of dialysis	4.00±4.02	3.94±4.01
Type of dialysis		
Hemodialysis	1652 (93%)	1633 (92%)
Peritoneal dialysis	137 (7%)	143 (8%)
Combination	17 (1%)	18 (1%)

N Engl J Med 2021;384:1601-1612

PRISMA HEALTH.

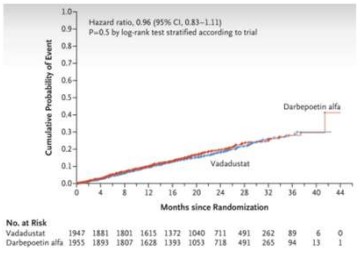
90

Vadadustat (Vafseo®)

INNO2VATE-1&2
(n=3923)

Adults with CKD on HD

1° Endpoints:
the first occurrence of an adjudicated major adverse cardiovascular event (MACE) — pooled across the two trials.



N Engl J Med 2021;384:1601-1612

N Engl J Med 2021;384:1601-1612

PRISMA HEALTH.

91

Vadadustat (Vafseo®)

Contraindications & Precautions

- Hepatotoxicity
  - Monitor ALT, AST and bilirubin monthly for the first 6 months
- Hypertension
  - Monitor blood pressure. Adjust anti-hypertensive therapy as needed
- Seizures
- Gastrointestinal Erosion
- Malignancy
  - Not recommended with active malignancy.

Vafseo package insert from Akebia Therapeutics, revised March 2024

PRISMA HEALTH.

92

Vadadustat (Vafseo®)

Pregnancy
- Risks to the mother and fetus associated with CKD

Lactation
- Not recommended (may resume 2 days after last dose)

Pediatric
- Safety and effectiveness not established

Geriatric
- No overall differnece in saftey or effectivness obeserved in patients greater than 65 when compared to younger population

Vafseo package insert from Akebia Therapeutics, revised March 2024

PRISMA HEALTH.

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Vadadustat (Vafseo®)

Copay Cards

- Unknown

Patient Assistance

- Unknown

Vafseo package insert from Akebia Therapeutics, revised March 2024

PRISMA HEALTH.

94

Infectious Diseases

PRISMA HEALTH.

95

sef-toe-bye-prole me-DOK-a-ril (Zev-tear-ah)

Ceftobiprole medocaril sodium (Zevtera®)

Indicated to treat certain bloodstream infections, bacterial skin and associated tissue infections, and community-acquired bacterial pneumonia

- Mechanism of action: cephalosporin with bactericidal activity by inhibition of bacterial cell wall synthesis
  - activity against gram-positive and gram-negative bacteria, including methicillin-resistant and susceptible Staphylococcus aureus.
    - high affinity for S. aureus PBPs 1 – 4,
    - PBP2a in methicillin-resistant Staphylococcus aureus
    - PBP2x and PBP2b in penicillin-resistant Streptococcus pneumoniae.
  - not active against gram-negative bacteria producing extended-spectrum β-lactamases (ESBLs)

FDA Approval: April 2024

PRISMA HEALTH.

96

Ceftobiprole medocaril sodium (Zevtera®)

Indicated to treat certain bloodstream infections, bacterial skin and associated tissue infections, and community-acquired bacterial pneumonia

Indication (Adults)	Dose	Frequency
SAB	667 mg	Every 6 hours on Days 1 to 8
		Every 8 hours from Day 9
ABSSSI	667 mg	Every 8 hours
CABP	667 mg	Every 8 hours

ABSSSI: Acute bacterial skin and skin structure infections; CABP: Community acquired bacterial pneumonia; SAB: Staphylococcus aureus bacteremia

Zeftera package insert from Basilea, revised April 2024

PRISMA HEALTH.

97

Ceftobiprole medocaril sodium (Zevtera®)

Indicated to treat certain bloodstream infections, bacterial skin and associated tissue infections, and community-acquired bacterial pneumonia (CABP)

Pediatric Age Group for CABP	Dose	Frequency
12 years to less than 18 years old	13.3 mg/kg (Max: 667 mg/dose)	Every 8 hours
≥ 3 months to less than 12 years	20 mg/kg (Max: 667 mg/dose)	Every 8 hours

Zeftera package insert from Basilea, revised April 2024

PRISMA HEALTH.

98

Ceftobiprole medocaril sodium (Zevtera®)

ERADICATE
(n=387)

Adults hospitalized with complicated S. *aureus* bacteremia

1º Endpoints:
Overall treatment success 70 days post randomization

Overall Demographics	Ceftobiprole (n=189)	Daptomycin (n=198)
Age, median (range)	57 (20-89)	58 (19-91)
Race		
White	179 (95%)	192 (97)
Black	4 (2%)	5 (2)
Other	6 (3%)	1(1)
Median duration of therapy, days (IQR)	21 (21-25)	21 (21-23)

N Engl J Med 2023;389:1390-1401

PRISMA HEALTH.

99

Ceftobiprole medocaril sodium (Zevtera®)

	Ceftobiprole	Daptomycin
Overall treatment success	132 (70%)	136 (69%)
Adjusted treatment difference 95%	2.0	
95% Confidence Interval	-7.1 to 11.1	
Noninferiority margin	-15%	

N Engl J Med 2023;389:1390-1401

PRISMA HEALTH.

100

Ceftobiprole medocaril sodium (Zevtera®)

TARGET
(n=679)

Adults with ABSSSI with a lesion area of at least 75 cm^2, systemic or regional signs of infection, and a requirement for IV antibiotic treatment.

1° Endpoints:
Clinical response 48-72 hours after start of Tx

Overall Demographics	Ceftobiprole (n=335)	Vanc/Azt (n=344)
Age, median (range)	51 (18-89)	50 (20-87)
Race, white	318 (95%)	330 (96)
Gender, male	198 (59.1)	201 (58.4)
Type of ABSSSI, n (%)		
Wound Infection	127 (38)	140 (41)
Cellulitis/erysipelas	112 (33)	111 (32.3)
Major abscess	96 (29)	93 (27)

Clin Infect Dis 2021 Oct 5;73(7):e1507-e1517

PRISMA HEALTH.

101

Ceftobiprole medocaril sodium (Zevtera®)

	Ceftobiprole	Vanc/Azt
Early clinical response	306 (91%)	303 (88%)
Adjusted treatment difference 95%	3.3	
95% Confidence Interval	-1.2 to 7.8	
Noninferiority margin	-10%	

Clin Infect Dis 2021 Oct 5;73(7):e1507-e1517

PRISMA HEALTH.

102

Ceftobiprole medocaril sodium (Zevtera®)

Bosheva et al (n=138)

Patients 3 months to <18 years old with HAP or CAP requiring hospitalization

1° Endpoints: cumulative incidence of AEs during the first 3 days of study treatment and at the EOT

Overall Demographics

	Ceftobiprole (n=94)	SoC Cephalosporin (n=44)
Age, median (range)	5 (0.6-17)	6 (1-17)
Race, white	94 (100%)	43 (98%)
Gender, male	53 (57%)	21 (48%)
Type of Pneumonia, n (%)		
CAP	89 (95%)	41 (93%)
HAP	5 (5%)	3 (7%)

Pediatr Infect Dis J. 2021 Jun 1;40(6):e222-e229

PRISMA HEALTH.

103

Ceftobiprole medocaril sodium (Zevtera®)

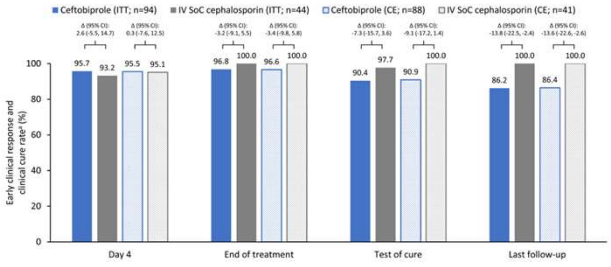
	First 3 days of IV therapy		While on IV therapy	
	Ceftobiprole	SOC Ceph.	Ceftobiprole	SOC Ceph.
Any AE	11 (12%)	5 (11%)	19 (20%)	8 (18%)
Treatment related AE	6 (6%)	0	8 (7%)	0
Severe AE	1 (1%)	0	1 (1%)	0
AE leading to discontinuation	2 (2%)	0	4 (4%)	0

Pediatr Infect Dis J. 2021 Jun 1;40(6):e222-e229

PRISMA HEALTH.

104

Ceftobiprole medocaril sodium (Zevtera®)



Pediatr Infect Dis J. 2021 Jun 1;40(6):e222-e229

PRISMA HEALTH.

105

Ceftobiprole medocaril sodium (Zevtera®)

Contraindications & Precautions

- Increased Mortality with Unapproved use in Ventilator-Associated Bacterial Pneumonia (VABP)
- Hypersensitivity Reactions
- Seizures and other adverse central nervous system (CNS) reactions
- Risk of Clostridioides difficile-associated diarrhea (CDAD)

Zeftera package insert from Basilea, revised April 2024

106

Ceftobiprole medocaril sodium (Zevtera®)

Contraindications & Precautions

- Adverse Reactions
  - Adult Patients
    - nausea, vomiting, diarrhea
    - headache, insomnia, dizziness
    - hepatic enzyme increased, abdominal pain
    - phlebitis, hypertension
  - Pediatric Patients:
    - vomiting, headache, diarrhea
    - infusion site reaction, pyrexia
    - hepatic enzyme increased

Zeftera package insert from Basilea, revised April 2024

107

Ceftobiprole medocaril sodium (Zevtera®)

Pregnancy
- No data available

Lactation
- No data available

Pediatric
- Safety and effectiveness have been established for the treatment of CABP in pediatric patients ≥ 3 months

Geriatric
- No overall difference in safety or effectiveness observed in patients greater than 65 when compared to younger population

Zeftera package insert from Basilea, revised April 2024

108

Ceftobiprole medocaril sodium (Zevtera®)

Copay Cards

- Unknown/Not Applicable
- Inpatient medication

Patient Assistance

- Unknown/Not Applicable
- Inpatient medication

Zeftera package insert from Basilea, revised April 2024

PRISMA HEALTH.

109

Soo-loe-PEN-em et-za-DROX-il proe-BEEN-e-sid (ORE-lin-vuh)

Sulopenem etzadroxil, probenecid (Orlynvah™)

Indicated to treat uncomplicated urinary tract infections (uUTI)

- Mechanism of action:
  - Sulopenem etzadroxil, the prodrug of intravenous sulopenem, is an oral thiopenem with activity similar to ertapenem
  - Probenecid extends plasma half-life by delaying clearance of sulopenem
- Targeted microorganisms include
  - *Escherichia coli*
  - *Klebsiella pneumoniae*
  - *Proteus mirabilis*

FDA Approval: October 2024

PRISMA HEALTH.

110

Sulopenem etzadroxil, probenecid (Orlynvah™)

Indicated to treat uncomplicated urinary tract infections (uUTI)

- Dose: Sulopenem etzadroxil 500 mg and Probenecid 500 mg orally twice daily
  - Duration for 5 days
- Renal function: not recommended with CrCl < 15 mL/min or with hemodyalisis

Orlynvah package insert from Iterum Therapeutics, revised October 2024

PRISMA HEALTH.

111

Sulopenem etzadroxil, probenecid (Orlynvah™)

Dunne et al.
(MITT; n=1579)

Women ≥18 years with UUTIs defined by a urinalysis positive for nitrite and either a positive leukocyte esterase or microscopic evidence of white blood cells, and ≥2 signs/symptoms of uUTI

1° Endpoints:
Combined clinical and microbiological response on day 12 in the mMITT-S & mMITT-R populations

Baseline Characteristics (mMITT-R)

	Sulopenem (N=147)	Ciprofloxacin (N=139)
Age, mean (SD)	54.5 (19.3)	56.3 (20.1)
Race		
White	130 (88.4)	126 (90.6)
Black	14 (9.5)	12 (8.6)
Other	3 (2.0)	1 (0.7)
BMI, mean (SD)	28.3 (7.1)	28.6 (6.4)
CrCl, mean (SD)	74.4 (28.2)	71.0 (28.2)

Clin Inf Dis 2023;76(1):66–77 mMITT-S, mMITT-R :modified intention to treat resistant, susceptible to ciprofloxacin

PRISMA HEALTH.

112

Sulopenem etzadroxil, probenecid (Orlynvah™)

Dunne et al.
(MITT; n=1579)

Women ≥18 years with UUTIs defined by a urinalysis positive for nitrite and either a positive leukocyte esterase or microscopic evidence of white blood cells, and ≥2 signs/symptoms of uUTI

1° Endpoints:
Combined clinical and microbiological response on day 12 in the mMITT-S & mMITT-R populations

Baseline Characteristics (mMITT-S)

	Sulopenem (N=370)	Ciprofloxacin (N=415)
Age, mean (SD)	50.9 (19.0)	49.9 (18.6)
Race		
White	330 (89.2)	376 (90.6)
Black	33 (8.9)	34 (8.2)
Other	7 (1.9)	5 (1.2)
BMI, mean (SD)	27.6 (6.7)	27.3 (6.4)
CrCl, mean (SD)	76.7 (27.4)	79.9 (25.0)

Clin Inf Dis 2023;76(1):66–77 mMITT-S, mMITT-R :modified intention to treat resistant, susceptible to ciprofloxacin

PRISMA HEALTH.

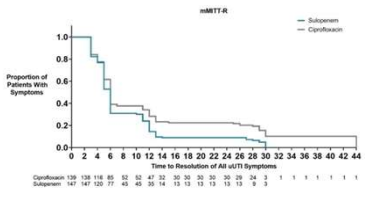
113

Sulopenem etzadroxil, probenecid (Orlynvah™)

Dunne et al.
(MITT; n=1579)

Women ≥18 years with UUTIs defined by a urinalysis positive for nitrite and either a positive leukocyte esterase or microscopic evidence of white blood cells, and ≥2 signs/symptoms of uUTI

1° Endpoints:
Combined clinical and microbiological response on day 12 in the mMITT-S & mMITT-R populations



J AM ACAD DERMATOL 2024

PRISMA HEALTH.

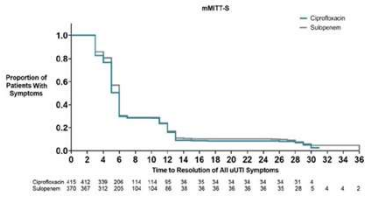
114

Sulopenem etzadroxil, probenecid (Orlynvah™)

Dunne et al.
(MITT; n=1579)

Women ≥18 years with UUTIs defined by a urinalysis positive for nitrite and either a positive leukocyte esterase or microscopic evidence of white blood cells, and ≥2 signs/symptoms of uUTI

1° Endpoints:
Combined clinical and microbiological response on day 12 in the mMITT-S & mMITT-R populations



J AM ACAD DERMATOL 2024

PRISMA HEALTH.

115

Sulopenem etzadroxil, probenecid (Orlynvah™)

Dunne et al.
(MITT; n=1579)

Women ≥18 years with UUTIs defined by a urinalysis positive for nitrite and either a positive leukocyte esterase or microscopic evidence of white blood cells, and ≥2 signs/symptoms of uUTI

1° Endpoints:
Combined clinical and microbiological response on day 12 in the mMITT-S & mMITT-R populations

Primary Efficacy End Point			
	Sulopenem (N=370)	Ciprofloxacin (N=415)	Absolute Difference (95% CI)
Combined clinical and microbiological response Day 12 (test of cure)			
MMITT-R	92/147 (62.6)	50/139 (36.0)	26.6 (15.1 to 37.4)
MMITT-S	247/370 (66.8)	326/415 (78.6)	-11.8 (-18.0 to −5.6)
mMITT	339/517 (65.6)	376/554 (67.9)	-2.3 (-7.9 to 3.3)

Clin Inf Dis 2023;76(1):66–77 mMITT-S, mMITT-R :modified intention to treat resistant, susceptible to ciprofloxacin

PRISMA HEALTH.

116

Sulopenem etzadroxil, probenecid (Orlynvah™)

Contraindications & Precautions

- Patients with known blood dyscrasias
- Patients with known blood dyscrasias
- Patients with known uric acid kidney stones
- Concomitant use with ketorolac is contraindicated

Orlynvah package insert from Iterum Therapeutics, revised October 2024

PRISMA HEALTH.

117

Sulopenem etzadroxil, probenecid (Orlynvah™)

Contraindications & Precautions

- Adverse Reactions
  - *Clostridioides difficile*-associated Diarrhea (CDAD)
  - Exacerbation of Gout

Orlynvah package insert from Iterum Therapeutics, revised October 2024

PRISMA HEALTH.

118

Sulopenem etzadroxil, probenecid (Orlynvah™)

Pregnancy
- Insufficient data to evaluate risk for adverse maternal or fetal outcomes

Lactation
- No data on presence in human milk. Not recommended while breast feeding

Pediatric
- Safety and effectiveness not established

Geriatric
- No overall difference in safety or effectiveness observed in patients greater than 65 when compared to younger population

Orlynvah package insert from Iterum Therapeutics, revised October 2024

PRISMA HEALTH.

119

Sulopenem etzadroxil, probenecid (Orlynvah™)

Copay Cards
- Unknown/Not Applicable
- Inpatient medication

Patient Assistance
- Unknown/Not Applicable
- Inpatient medication

Orlynvah package insert from Iterum Therapeutics, revised October 2024

PRISMA HEALTH.

120

Neurology/Psychiatry

PRISMA HEALTH.

121

Donanemab-azbt (Kisunla™)

Duh-NAH-nuh-mab
(kih-SUHN-lah)

Indicated to treat Alzheimer's disease

- Mechanism of action: humanized immunoglobulin gamma 1 (IgG1) monoclonal antibody directed against insoluble N-truncated pyroglutamate amyloid beta.
  - reduces amyloid beta plaques, as evaluated in Study 1

Boxed Warning: Amyloid related imaging abnormalities

FDA Approval: July 2024

PRISMA HEALTH.

122

Donanemab-azbt (Kisunla™)

Indicated to treat Alzheimer's disease

Intravenous Infusion (every 4 weeks)	Dosage (administered over 30 minutes)
Infusion 1, 2, and 3	700 mg
Infusion 4 and beyond	1400 mg

If dose is missed: resume scheduled dose every 4 weeks ASAP

Kisunla package insert from Eli Lilly and Company, revised July 2024

PRISMA HEALTH.

123

Donanemab-azbt (Kisunla™)

TRAILBLAZER-ALZ 2 (n=1736)

Adults with confirmed presence of amyloid pathology and mild cognitive impairment or dementia , consistent with Stage 3 & 4 Alzheimer's disease

1° Endpoints: change in the iADRS score from baseline to 76 weeks

Overall Demographics

		Donanemab (n=860)	Placebo (n=876)
Age, mean ± SD		73±6.2	73±6.2
Race			
	White	781 (91)	807 (93)
	Black	19 (2)	21 (2)
	Asian	57 (7)	47 (5)
	iADRS score	104.1±14.3	103.6±14.0
APOE carrier			
	E3/E3	241 (28)	230 (26)
	E3/E4	433 (50)	450 (52)
	E4/E4	143 (17)	146 (17)

iADRS: Integrated Alzheimer's Disease Rating Scale

JAMA 2023 Aug 8;330(6):512-527

PRISMA HEALTH.

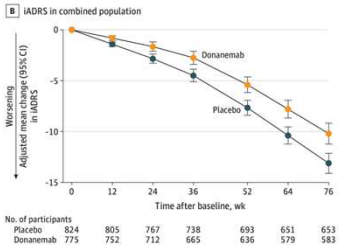
124

Donanemab-azbt (Kisunla™)

TRAILBLAZER-ALZ 2 (n=1736)

Adults with confirmed presence of amyloid pathology and mild cognitive impairment or dementia , consistent with Stage 3 & 4 Alzheimer's disease

1° Endpoints: change in the iADRS score from baseline to 76 weeks



iADRS: Integrated Alzheimer's Disease Rating Scale

JAMA 2023 Aug 8;330(6):512-527

PRISMA HEALTH.

125

Donanemab-azbt (Kisunla™)

Contraindications & Precautions

- Amyloid Related Imaging Abnormalities (ARIA):
  - Enhanced clinical vigilance for ARIA is recommended during the first 24 weeks of treatment
- Infusion-Related Reactions
  - The infusion rate may be reduced, or the infusion may be discontinued, and appropriate therapy initiated as clinically indicated
  - Consider pre-treatment with antihistamines, acetaminophen, or corticosteroids prior to subsequent dosing

Kisunla package insert from Eli Lilly and Company, revised July 2024

PRISMA HEALTH.

126

Donanemab-azbt (Kisunla™)

Pregnancy
- No data available

Lactation
- No data available

Pediatric
- Safety and effectiveness not established

Geriatric
- No overall difference in safety or effectiveness observed in patients greater than 65 when compared to younger population

Kisunla package insert from Eli Lilly and Company, revised July 2024

PRISMA HEALTH.

127

Donanemab-azbt (Kisunla™)

Copay Cards
- Unknown

Patient Assistance
- Lilly Cares Foundation
- https://www.lillycares.com/

Kisunla package insert from Eli Lilly and Company, revised July 2024

PRISMA HEALTH.

128

Zuh-NOM-a-leen TROS-pee-um (Co-BEEN-fee)

Xanomeline and trospium chloride (Cobenfy™)

Indicated to treat schizophrenia

Mechanism of action: thought to be due to its agonist activity at M1 and M4 muscarinic acetylcholine receptors in the central nervous system
- Xanomeline: muscarinic agonist
- Trospium chloride: muscarinic antagonist

FDA Approval: September 2024

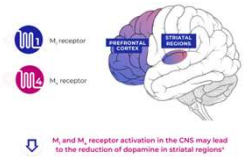
PRISMA HEALTH.

129

Zuh-NOM-a-leen TROS-pee-um
(Co-BEEN-fee)

Xanomeline and trospium chloride (Cobenfy™)

Indicated to treat schizophrenia



- Xanomeline: selective activates M1 and M4 in the CNS
- Trospium chloride antagonizes muscarinic receptors primary in peripheral tissues

FDA Approval: September 2024

PRISMA HEALTH.

130

Xanomeline and trospium chloride (Cobenfy™)

Indicated to treat schizophrenia

Initial	Followed By	Then
•50 mg/20 mg capsule twice daily for ≥2 days	• 100 mg/20 mg capsule twice daily ≥ 5 days	•125 mg/30 mg twice daily based on tolerability

Prior to initiation of Xanomeline and trospium chloride
- Assess liver enzymes and bilirubin
- Assess heart rate at baseline

Cobenfy package insert from Bristol-Myers Squibb, revised September 2024

PRISMA HEALTH.

131

Xanomeline and trospium chloride (Cobenfy™)

EMERGENT-2
(mITT; n=236)

Adults 18-65 years with Schizophrenia, acute exacerbation with onset < 2 months prior to screening and a PANNS score of 80-120

1° Endpoints:
Change from baseline to week 5 in PANSS score

Baseline Demographics (mITT)

	KarXT (n=117)	Placebo (n=119)
Age, mean (SD)	45.9 (10.4)	46.1 (10.8)
Race		
White	23 (20)	31 (26)
Black	91 (78)	86 (72)
Asian	2 (2)	0 (0)
Female	30 (26)	28 (23)
PANSS score, mean (SD)	98.2 (8.9)	97.7 (9.4)

Lancet 2024; 403:160–70 PANNS: Positive and Negative Syndrome Scale

PRISMA HEALTH.

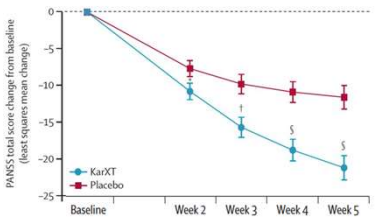
132

Xanomeline and trospium chloride (Cobenfy™)

EMERGENT-2
(mITT; n=236)

Adults 18-65 years with Schizophrenia, acute exacerbation with onset < 2 months prior to screening and a PANNS score of 80-120

1° Endpoints:
Change from baseline to week 5 in PANSS score



Lancet 2024; 403:160–70 PANNS: Positive and Negative Syndrome Scale

133

Xanomeline and trospium chloride (Cobenfy™)

Kaul et al
(ITT; n=256)

Adults 18-65 years with Schizophrenia and a PANNS score of 80-120

1° Endpoints:
Change from baseline to week 5 in PANSS score in mITT population

Baseline Demographics (ITT)

	Xanomeline-trospium (n=125)	Placebo (n=131)
Age, mean (SD)	43.6 (11.4)	42.6 (12.2)
Race		
White	45 (36)	53 (40.5)
Black	79 (63.2)	77 (58.8)
Asian	1 (0.8)	0 (0)
Female	38 (30.4)	27 (20.6)
PANSS score, mean (SD)	97.3 (8.9)	96.7 (8.9)

JAMA Psychiatry. 2024;81(8):749-756 PANNS: Positive and Negative Syndrome Scale

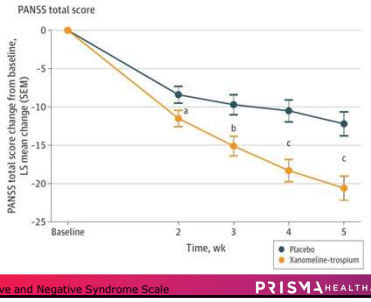
134

Xanomeline and trospium chloride (Cobenfy™)

Kaul et al
(mITT; n=234)

Adults 18-65 years with Schizophrenia and a PANNS score of 80-120

1° Endpoints:
Change from baseline to week 5 in PANSS score in mITT population



JAMA Psychiatry. 2024;81(8):749-756 PANNS: Positive and Negative Syndrome Scale

135

Xanomeline and trospium chloride (Cobenfy™)

Contraindications & Precautions

- Urinary retention
- Moderate or severe hepatic impairment
- Gastric Retention
- Untreated narrow-angle glaucoma

Cobenfy package insert from Bristol-Myers Squibb, revised September 2024

PRISMA HEALTH.

136

Xanomeline and trospium chloride (Cobenfy™)

Contraindications & Precautions

- Adverse Reactions
  - Anticholinergic
  - Angioedema
  - CNS depression
  - Hypertension
  - Nausea, vomiting, constipation, abdominal pain

Cobenfy package insert from Bristol-Myers Squibb, revised September 2024

PRISMA HEALTH.

137

Xanomeline and trospium chloride (Cobenfy™)

Pregnancy
- Insufficient data to evaluate risk for adverse maternal or fetal outcomes

Lactation
- No data on presence in human milk. Not recommended while breast feeding

Pediatric
- Safety and effectiveness not established

Geriatric
- No data available (clinical trials did not include significant number of patients > 65 years)

Cobenfy package insert from Bristol-Myers Squibb, revised September 2024

PRISMA HEALTH.

138

Xanomeline and trospium chloride (Cobenfy™)

Copay Cards

- As low as $0 per month
- www.cobenfy.com/support-program

Patient Assistance

- Bristol-Myers Squibb Patient Assistance Foundation (BMS PAF)
- https://www.bmspaf.org/#/home

Cobenfy package insert from Bristol-Myers Squibb, revised September 2024

PRISMA HEALTH.

139

Miscellaneous

PRISMA HEALTH.

140

RES-me-TIR-om
(rez-di-frah)

Resmetirom (Rezdiffra™)

Indicated to treat noncirrhotic non-alcoholic steatohepatitis with moderate to advanced liver fibrosis

- Mechanism of action: partial agonist of the thyroid hormone receptor-beta (THR-β)
  - THR-β is the major form of THR in the liver
    - Stimulation of THR-β in the liver reduces intrahepatic triglycerides,
  - THR-α is the main mediator outside the liver, including in heart and bone

FDA Approval:March 2024

PRISMA HEALTH.

141

Resmetirom (Rezdiffra™)

Indicated to treat noncirrhotic non-alcoholic steatohepatitis with moderate to advanced liver fibrosis

- The recommended dosage of REZDIFFRA is based on actual body weight
  - <100 kg, the recommended dosage is 80 mg orally once daily
  - ≥100 kg, the recommended dosage is 100 mg orally once daily
- Administer REZDIFFRA with or without food.

Rezdiffra package insert from Madrigal Pharmaceuticals, revised March 2024

PRISMA HEALTH.

142

Resmetirom (Rezdiffra™)

MAESTRO-NASH (n=966)

Adults with at least 3 metabolic risk factors, histologic evidence of NASH, & NAFLD activity score ≥ 4

1° Endpoints:
NASH resolution and an improvement in fibrosis by at least one stage at week 52

Overall Demographics

	Resmetirom 80 mg (n=322)	Resmetirom 100 mg (n=323)	Placebo (n=321)
Age, mean ± SD	55.9±11.5	57.0±10.8	57.1±10.5
Race			
White	291 (90)	291 (90)	281 (88)
Black	5 (2)	5 (2)	9 (3)
Other	12 (4)	11 (4)	18 (6)
NAFLD score ≥5	266 (83)	288 (89)	253 (79)

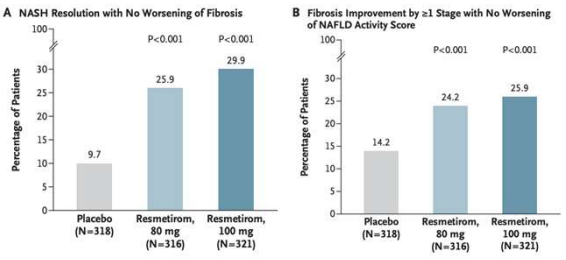
N Engl J Med 2024;390:497-509

NAFLD: nonalcoholic fatty liver disease

PRISMA HEALTH.

143

Resmetirom (Rezdiffra™)



N Engl J Med 2024;390:497-509

PRISMA HEALTH.

144

Resmetirom (Rezdiffra™)

	Resmetirom 80 mg vs Placebo, % pts	P-value	Resmetirom 100 mg vs Placebo, % pts	P-value
NASH resolution with no worsening of fibrosis	16.4 (11.0–21.8)	<0.001	20.7 (15.3–26.2)	<0.001
Fibrosis improvement by ≥1 stage with no worsening of NAFLD activity score	10.2 (4.8–15.7)	<0.001	11.8 (6.4–17.2)	<0.001

N Engl J Med 2024;390:497-509

PRISMA HEALTH.

145

Resmetirom (Rezdiffra™)

Contraindications & Precautions

- Hepatotoxicity
  - Discontinue REZDIFFRA and continue to monitor the patient if hepatotoxicity is suspected
- Gallbladder-Related Adverse Reactions
  - If cholelithiasis is suspected, gallbladder diagnostic studies and appropriate clinical follow-up are indicated
  - If an acute gallbladder event such as acute cholecystitis is suspected, interrupt REZDIFFRA treatment until the event is resolved

Rezdiffra package insert from Madrigal Pharmaceuticals, revised March 2024

PRISMA HEALTH.

146

Resmetirom (Rezdiffra™)

Contraindications & Precautions

- Adverse Reactions
  - Diarrhea, nausea, vomiting, constipation, abdominal pain
  - Dizziness
  - Pruritis
- Major Drug Interactions
  - Strong CYP2C8 Inhibitors: use not recommended
  - Moderate CYP2C8 Inhibitors: reduce REZDIFFRA dosage
  - OATP1B1 and OATP1B3 Inhibitors: not recommended.
  - Atorvastatin, Pravastatin, Rosuvastatin and Simvastatin: Limit statin dosage
  - CYP2C8 Substrates: Monitor for substrate related adverse reactions.

Rezdiffra package insert from Madrigal Pharmaceuticals, revised March 2024

PRISMA HEALTH.

147

Resmetirom (Rezdiffra™)

Pregnancy
- No data available

Lactation
- No data available

Pediatric
- Safety and effectiveness not established

Geriatric
- No overall difference in safety or effectiveness observed in patients greater than 65 when compared to younger population

Rezdiffra package insert from Madrigal Pharmaceuticals, revised March 2024

PRISMA HEALTH.

148

Resmetirom (Rezdiffra™)

Copay Cards
- As low as $10 per month
- https://portal.trialcard.com/madrigal/rezdiffra/landing/

Patient Assistance
- Madrigal Patient Support
- https://madrigalpatientsupport.com/patient/financial-assistance-patient/https://madrigalpatientsupport.com/patient/financial-assistance-patient/

Rezdiffra package insert from Madrigal Pharmaceuticals, revised March 2024

PRISMA HEALTH.

149

Do-RUX-oh-LI-ti-nib (lek-sel-vee)

Deuruxolitinib (Leqselvi™)

Indicated to treat adult patients with severe alopecia areata.

- Mechanism of action: Janus kinase (JAK) inhibitor.
  - JAKs mediate the signaling of cytokines and growth factors that are important for hematopoiesis and immune function.

Boxed Warning: serious infections, mortality, malignancy, major adverse cardiovascular events (mace) and thrombosis

FDA Approval: July 2024

PRISMA HEALTH.

150

Deuruxolitinib (Leqselvi™)

Indicated to treat adult patients with severe alopecia areata.

- Dose: 8 mg orally twice daily
- May take with or without food
- If a dose is missed, skip the missed dose and resume the next scheduled dose

Boxed Warning: serious infections, mortality, malignancy, major adverse cardiovascular events (mace) and thrombosis

Leqselvi package insert from Sun Pharmaceutical Industries, revised July 2024

PRISMA HEALTH.

151

Deuruxolitinib (Leqselvi™)

THRIVE AA-1 (n=706)

Adults 18-65 years with ≥50% scalp hair loss and a current episode of scalp hair loss of AA lasting between 6 months and 10 years

1° Endpoints: percentage of patients who achieved a SALT score ≤ 20 at week 24

Overall Demographics

	Deu 12 mg (n=215)	Deu 8 mg (n=351)	Placebo (n=140)
Age, median (range)	36 (18-65)	37 (18-65)	38.5 (8-65)
Race			
White	145 (67)	241 (69)	98 (70)
Black	27 (13)	40 (11)	16 (11)
Asian	21 (10)	22 (6)	10 (7)
Female	131 (61)	217 (62)	89 (64)
SALT score, mean± SD	85.2 ±18.4	85.5±18.4	88.1±15.1

J AM ACAD DERMATOL 2024 SALT: serverity of alopecia tool

PRISMA HEALTH.

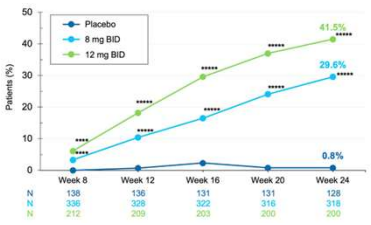
152

Deuruxolitinib (Leqselvi™)

THRIVE AA-1 (n=706)

Adults 18-65 years with ≥50% scalp hair loss and a current episode of scalp hair loss of AA lasting between 6 months and 10 years

1° Endpoints: percentage of patients who achieved a SALT score ≤ 20 at week 24



J AM ACAD DERMATOL 2024

PRISMA HEALTH.

153

Deuruxolitinib (Leqselvi™)

Contraindications & Precautions

- LEQSELVI is contraindicated in patients:
  - Who are CYP2C9 poor metabolizers
  - Using moderate or strong CYP2C9 inhibitors.

Boxed Warning: serious infections, mortality, malignancy, major adverse cardiovascular events (mace) and thrombosis

Leqselvi package insert from Sun Pharmaceutical Industries, revised July 2024 PRISMA HEALTH.

154

Deuruxolitinib (Leqselvi™)

Contraindications & Precautions

- Gastrointestinal Perforations
  - Evaluate promptly patients presenting with new onset abdominal symptoms
- Lipid Elevations,
- Anemia, Neutropenia, and Lymphopenia
- Immunizations
  - Avoid use of live vaccines during or immediately prior to use
- Drug interactions
  - Strong CYP3A4 and moderate or strong CYP2C9 inducers: Avoid use

Leqselvi package insert from Sun Pharmaceutical Industries, revised July 2024 PRISMA HEALTH.

155

Deuruxolitinib (Leqselvi™)

Contraindications & Precautions

- Adverse Reactions
  - Headache
  - Acne
  - Nasopharyngitis
  - Fatigue,
  - Weight increased,
  - lymphopenia, thrombocytosis, anemia, neutropenia,
  - skin and soft tissue infections, herpes.

Leqselvi package insert from Sun Pharmaceutical Industries, revised July 2024 PRISMA HEALTH.

156

Deuruxolitinib (Leqselvi™)

Pregnancy
- Fetal harm found in animal reproduction studies

Lactation
- Breastfeeding is not recommended (May resume 1 day after last dose)

Pediatric
- Safety and effectiveness not established

Geriatric
- No data available (clinical trials did not include significant number of patients > 65 years)

Leqselvi package insert from Sun Pharmaceutical Industries, revised July 2024

PRISMA HEALTH.

157

Deuruxolitinib (Leqselvi™)

Copay Cards
- Unknown

Patient Assistance
- Unknown
- May contact manufacturer

Leqselvi package insert from Sun Pharmaceutical Industries, revised July 2024

PRISMA HEALTH.

158

leb-ri-KIZ-ue-mab-lbkz
(Ehb-glis)

Lebrikizumab-lbkz (Ebglyss™)

Indicated to treat moderate-to-severe atopic dermatitis

- Mechanism of action: IgG4 monoclonal antibody that binds with high affinity and slow off-rate to interleukin (IL)-13
  - allows IL-13 to bind to IL-13Rα1
  - inhibits human IL-13 signaling through the IL-4Rα/IL-13Rα1 receptor complex

FDA Approval: September 2024

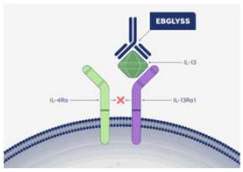
PRISMA HEALTH.

159

leb-ri-KIZ-ue-mab-lbkz
(Ehb-glis)

Lebrikizumab-lbkz (Ebglyss™)

Indicated to treat moderate-to-severe atopic dermatitis



- Selectively binds to IL-13, preventing formation of IL-Ra/IL-13Ra1 complex
- Neutralizes IL-13 with high binding affinity and slow dissociation

FDA Approval: September 2024

160

Lebrikizumab-lbkz (Ebglyss™)

Indicated to treat moderate-to-severe atopic dermatitis

Initial	Followed By	Maintenance
•500 mg Week 0 •500 mg Week 2	• 250 mg every two weeks •at least week 16 •adequate clinical response is achieved.	•250 mg every four weeks

Ebglyss package insert from Eli Lilly, revised September 2024

161

Lebrikizumab-lbkz (Ebglyss™)

Blauvelt et al.
(n=284)

Patients aged ≥ 12 years and weighing ≥ 40 kg with moderate-to-severe AD and a history of inadequate response or inability to utilize topical therapies

1° Endpoints:
Percentage of patients who maintained EASI response at 52 weeks

What we already know prior to this trial

- At 16 weeks lebrikizumab was found to be safe
- At 16 weeks lebrikizumab achieved statistically significant and clinically meaningful improvements

Br J Dermatol 2023; 188:740–748 EASI: Eczema Area and Severity Index

162

Lebrikizumab-lbkz (Ebglyss™)

Blauvelt et al.
(n=284)

Patients aged ≥ 12 years and weighing ≥ 40 kg with moderate-to-severe AD and a history of inadequate response or inability to utilize topical therapies

1° Endpoints:
Percentage of patients who maintained EASI response at 52 weeks

Baseline Demographics

	Placebo (n=60)	Leb Q4W (n=118)	Leb Q2W (n=113)
Age, median (SD)	33.8 (16.6)	35.8 (17.3)	36.1 (17)
Race			
White	33 (55)	86 (72.9)	80 (70.8)
Black	8 (13.3)	12 (10.2)	9 (8.0)
Asian	15 (25)	17 (14.4)	19 (16.8)
Female	36 (60)	69 (58.5)	53 (46.9)
EASI score, mean± SD	28.9 (11.2)	28.8 (12.6)	29.5 (10.8)

Br J Dermatol 2023; 188:740–748

PRISMA HEALTH.

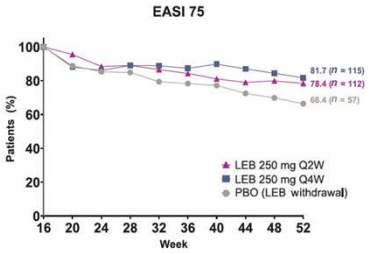
163

Lebrikizumab-lbkz (Ebglyss™)

Blauvelt et al.
(n=284)

Patients aged ≥ 12 years and weighing ≥ 40 kg with moderate-to-severe AD and a history of inadequate response or inability to utilize topical therapies

1° Endpoints:
Percentage of patients who maintained EASI response at 52 weeks



Br J Dermatol 2023; 188:740–748

PRISMA HEALTH.

164

Lebrikizumab-lbkz (Ebglyss™)

Simpson et al.
(n=284)

Patients aged ≥ 12 years and weighing ≥ 40 kg with moderate-to-severe AD and a history of inadequate response or inability to utilize topical therapies

1° Endpoints:
Percentage of patients with an IGA score of ≤1, and a ≥ 2-point improvement from baseline at week 16

Baseline Demographics

	PBO + TCS (n=66)	LEB + TCS (n=145)
Age, mean (SD)	36.7 (17.9)	37.5 (19.9)
Race		
White	40 (60.6)	90 (62.1)
Black	9 (13.6)	19 (13.1)
Asian	13 (19.7)	18 (12.4)
Female	33 (50.0)	70 (48.3)
IGA 3	48 (72.7)	98 (67.6)
EASI score, mean (SD)	26.4 (10.6)	27.7 (11.1)

JAMA Dermatol. 2023;159(2):182-191

PRISMA HEALTH.

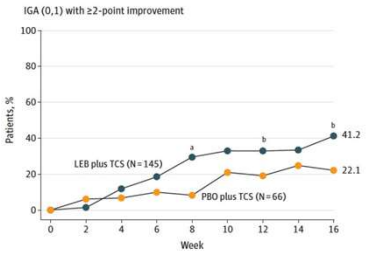
165

Lebrikizumab-lbkz (Ebglyss™)

Simpson et al. (n=284)

Patients aged ≥ 12 years and weighing ≥ 40 kg with moderate-to-severe AD and a history of inadequate response or inability to utilize topical therapies

1° Endpoints: Percentage of patients with an IGA score of ≤1, and a ≥ 2-point improvement from baseline at week 16



JAMA Dermatol. 2023;159(2):182-191

PRISMA HEALTH.

166

Lebrikizumab-lbkz (Ebglyss™)

Contraindications & Precautions

- Hypersensitivity reactions including angioedema and urticaria
- Conjunctivitis and Keratitis: Report new onset or worsening eye
- Increased risk of parasitic (Helminth) infections
- Avoid use of live vaccines during treatment

Ebglyss package insert from Eli Lilly, revised September 2024

PRISMA HEALTH.

167

Lebrikizumab-lbkz (Ebglyss™)

Pregnancy
- Insufficient data to evaluate risk for adverse maternal or fetal outcomes

Lactation
- No data on presence in human milk. Not recommended while breast feeding

Pediatric
- Safety and effectiveness established in pediatric patients ≥ 12 weighing ≥ 40kg

Geriatric
- No data available (clinical trials did not include significant number of patients > 65 years)

Ebglyss package insert from Eli Lilly, revised September 2024

PRISMA HEALTH.

168

Lebrikizumab-lbkz (Ebglyss™)

Copay Cards

- As low as $0 per 28 days
- As low as $25 per 28 days if not covered by insurance
- https://ebglyss.lilly.com/savings-support#savings

Patient Assistance

- Lilly Cares Foundation
- https://assets.needymeds.org/papforms/lilpae3263.pdf

Ebglyss package insert from Eli Lilly, revised September 2024

PRISMA HEALTH.

169

Crinecerfont (Crenessity™)

CRIN-es-er-FONT (CRIN-es-it-ee)

Indicated to treat classic congenital adrenal hyperplasia

- Mechanism of action: a selective corticotropin-releasing factor (CRF) type 1 receptor antagonist.
  - blocks the binding of CRF to CRF type 1 receptors in the pituitary but not CRF type 2 receptors.
  - Crinecerfont binding to CRF type 1 receptors inhibits adrenocorticotropic hormone (ACTH) secretion from the pituitary, thereby reducing ACTH-mediated adrenal androgen production.

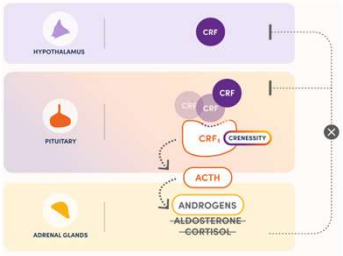
FDA Approval: December 2024

PRISMA HEALTH.

170

Crinecerfont (Crenessity™)

CRIN-es-er-FONT (CRIN-es-it-ee)



Cortisol deficieny leads to:

- Loss of negative feedback
- Increase in CRF
- Increase in CRF1 activation
- Increase in ACTH
- Overproduction of adrenal androgens

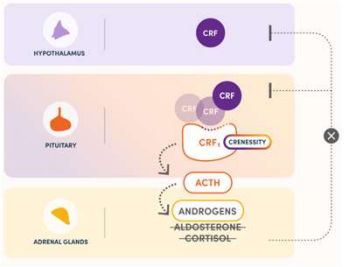
FDA Approval: December 2024

PRISMA HEALTH.

171

Crinecerfont (Crenessity™)

CRIN-es-er-FONT
(CRIN-es-it-ee)



Potent and selective CRF1 receptor antagonism leads to:
- Direct reduction in ACTH
- Reduction in downstream production of androgens

FDA Approval: December 2024

PRISMA HEALTH.

172

Crinecerfont (Crenessity™)

Indicated to treat classic congenital adrenal hyperplasia

Recommended Dosage for Pediatric Patients ≥ 4 years old	
Weight	**Dosage Regimen**
10 kg to less than 20 kg	25 mg orally twice daily
20 kg to less than 55 kg	50 mg orally twice daily
≥ 55 kg	100 mg orally twice daily

Dosage to be taken with a meal

Crenessity package insert from Neurocrine Biosciences, revised December 2024

PRISMA HEALTH.

173

Crinecerfont (Crenessity™)

CAHtalyst Adult (n=182)

Adults ≥18 years with CAH receiving a daily glucocorticoid dose of more than 13 mg/m3 of BSA of hydrocortisone equivalent

1° Endpoints: percentage change from baseline to week 24 in the daily dose of glucocorticoid

Baseline Characteristics		
	Crinecerfont (n=122)	Placebo (n=60)
Age, mean (SD)	31.3 (9.8)	29.8 (10.2)
White race	107 (88)	57 (95)
Male	61 (50)	31 (52)
Daily hydrocortisone equivalent, mg/day	32.4 (9.2)	32.1 (9.5)
Adjusted for BSA, mg/m2	17.5 (4.5)	17.9 (5.5)

N Engl J Med 391;6:504-514

PRISMA HEALTH.

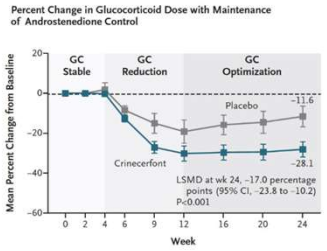
174

Crinecerfont (Crenessity™)

CAHtalyst Adult (n=182)

Adults ≥18 years with CAH receiving a daily glucocorticoid dose of more than 13 mg/m3 of BSA of hydrocortisone equivalent

1° Endpoints: percentage change from baseline to week 24 in the daily dose of glucocorticoid



N Engl J Med 391;6:504-514

PRISMA HEALTH.

175

Crinecerfont (Crenessity™)

CAHtalyst Pediatric (n=103)

Children 2 to 17 years with CAH receiving a total glucocorticoid dose of 12 mg/m2/day

1° Endpoints: Change in androstenedione level from baseline to week 4

Baseline Characteristics

	Crinecerfont (n=69)	Placebo (n=34)
Age, mean (SD)	12.0 (3.4)	12.1 (3.7)
White race	42 (61)	23 (68)
Male	35 (51)	18 (53)
Daily hydrocortisone equivalent, mg/m2/day	16.5 (4.2)	16.3 (3.4)

N Engl J Med 2024. 391(6):493-50

PRISMA HEALTH.

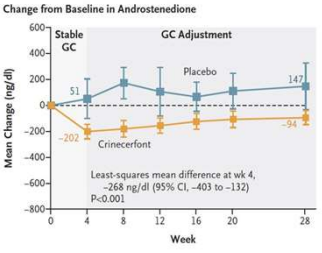
176

Crinecerfont (Crenessity™)

CAHtalyst Pediatric (n=103)

Children 2 to 17 years with CAH receiving a total glucocorticoid dose of 12 mg/m2/day

1° Endpoints: Change in androstenedione level from baseline to week 4



N Engl J Med 2024. 391(6):493-50

PRISMA HEALTH.

177

Crinecerfont (Crenessity™)

Contraindications & Precautions

- Hypersensitivity to crinecerfont or any excipient of CRENESSITY

Crenessity package insert from Neurocrine Biosciences, revised December 2024

PRISMA HEALTH.

178

Crinecerfont (Crenessity™)

Contraindications & Precautions

- Adverse Reactions
  - Fatigue
  - Headache
  - Dizziness
  - Arthralgias
  - Myalgias
  - Decrease appetite

Crenessity package insert from Neurocrine Biosciences, revised December 2024

PRISMA HEALTH.

179

Crinecerfont (Crenessity™)

Pregnancy

- Insufficient data to evaluate risk for adverse maternal or fetal outcomes

Lactation

- No data on presence in human milk. Not recommended while breast feeding

Pediatric

- Safety and effectiveness as adjunctive treatment to glucocorticoid replacement to control androgens established in pediatric patients 4 years of age and older

Geriatric

- No overall difference in safety or effectiveness observed in patients greater than 65 when compared to younger population

Crenessity package insert from Neurocrine Biosciences, revised December 2024

PRISMA HEALTH.

180

Crinecerfont (Crenessity™)

Copay Cards

- As low as $0 per month
- https://crenessity.neurocrineaccesssupport.com/patient/financial-assistance/

Patient Assistance

- https://crenessity.neurocrineaccesssupport.com/patient/financial-assistance/

Crenessity package insert from Neurocrine Biosciences, revised December 2024

PRISMA HEALTH.

181

Suzetrigine (Journavx™)

Su-ZEH-tre-geen
(Jur-NA-vix)

Indicated to treat moderate to severe acute pain in adults

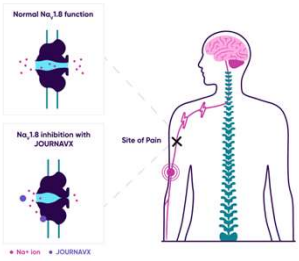
- Mechanism of action: a selective blocker of the NaV1.8 voltage-gated sodium channel
  - NaV1.8 is expressed in peripheral sensory neurons
    - NAV1.8's role is to transmit pain signals (action potentials)
    - inhibits transmission of pain signals to the brain

FDA Approval: January 2025

PRISMA HEALTH.

182

Suzetrigine (Journavx™)



- $Na_V1.8$ is a voltage-gated sodium channel that is selectively expressed in peripheral sensory neurons, where its role is to transmit pain signals
- $Na_V1.8$ is not expressed in the human brain
- **Not a controlled substance**
- **Not associated with addiction**

Journavx package insert from VERTEX, revised January 2025

PRISMA HEALTH.

183

Suzetrigine (Journavx™)

Indicated to treat moderate to severe acute pain in adults

Initial	12 hours later	Duration
• 100 mg orally • Take 1 hour before or 2 hours after food to avoid delay in onset of action	• 50 mg every 12 hours* • With or without food	• Use the shortest duration possible • Not studied beyond 14 days

* With moderate hepatic impairment: take first 5 doses as above, then take doses every 24 hours starting with dose 6.

Journavx package insert from VERTEX, revised January 2025

PRISMA HEALTH.

184

Suzetrigine (Journavx™)

Jones et al. Part 1 (n=182)

Adults 18-75 years who rated their pain as moderate to severe and reported ≥ 4 on the NPRS following abdominoplasty

1° Endpoints:
The time-weighted sum of the pain-intensity difference (SPID) over a period of 48 hr (SPID48)

Jones et al. Part 2 (n=182)

Adults 18-75 years who rated their pain as moderate to severe and reported ≥ 4 on the NPRS following bunionectomy

1° Endpoints:
The time-weighted sum of the pain-intensity difference (SPID) over a period of 48 hr (SPID48)

N Engl J Med 2023;389:393-405

PRISMA HEALTH.

185

Suzetrigine (Journavx™)

Baseline Characteristics (Abdominoplasty Trial)

	High-dose VX-548 (n=76)	Middle-dose VX-548 (n=74)	Hydrocodone-bitartrate-acetaminophen (n=76)	Placebo (n=77)
Age, mean (SD)	43.1 (9.7)	41.5 (9.2)	45.4 (10.7)	42.6 (9.5)
Race				
White	57 (75)	57 (77)	53 (70)	57 (74)
Black	13 (17)	15 (20)	18 (24)	20 (26)
Other	6 (8)	2 (3)	5 (7)	0 (0)
Female	75 (99)	74 (100)	73 (96)	76 (99)
VRS				
Moderate	44 (58)	45 (61)	45 (59)	42 (55)
Severe	32 (42)	29 (39)	31 (41)	35 (45)

N Engl J Med 2023;389:393-405

PRISMA HEALTH.

186

Suzetrigine (Journavx™)

Baseline Characteristics (Bunionectomy Trial)					
	High-dose VX-548 (n=60)	Mid-dose VX-548 (n=62)	Low-dose VX-548 (n=33)	Hydrocodone-bitartrate-acetaminophen (n=60)	Placebo (n=34)
Age, mean (SD)	47.6 (13.7)	48.3 (13.1)	47.8 (15.5)	50.0 (12.5)	47.8 (13.6)
Race					
White	42 (70)	44 (71)	22 (67)	44 (73)	41 (69)
Black	14 (23)	17 (27)	9 (27)	13 (22)	13 (22)
Other	4 (7)	1 (2)	2 (6)	3 (5)	5 (8)
Female	53 (88)	57 (92)	25 (76)	50 (83)	49 (83)
VRS					
Moderate	44 (73)	45 (73)	21 (64)	37 (62)	39 (66)
Severe	16 (27)	17 (27)	12 (36)	23 (38)	20 (34)

N Engl J Med 2023;389:393-405

PRISMA HEALTH.

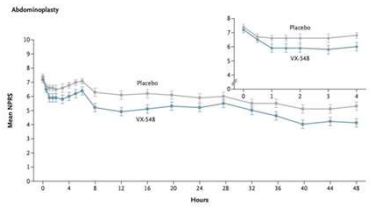
187

Suzetrigine (Journavx™)

Jones et al. Part 1 (n=303)

Adults 18-75 years who rated their pain as moderate to severe and reported ≥ 4 on the NPRS following abdominoplasty

1° Endpoints:
The time-weighted sum of the pain-intensity difference (SPID) over a period of 48 hr (SPID48)



N Engl J Med 2023;389:393-405

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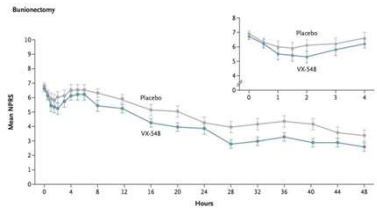
Suzetrigine (Journavx™)

Jones et al. Part 2 (n=274)

Adults 18-75 years who rated their pain as moderate to severe and reported ≥ 4 on the NPRS following bunionectomy

1° Endpoints:
The time-weighted sum of the pain-intensity difference (SPID) over a period of 48 hr (SPID48)



N Engl J Med 2023;389:393-405

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Suzetrigine (Journavx™)

Contraindications & Precautions

- Hypersensitivity to crinecerfont or any excipient of CRENESSITY
- Use with strong CYP3A inhibitors

Journavx package insert from VERTEX, revised January 2025

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Suzetrigine (Journavx™)

Contraindications & Precautions

- Adverse Reactions
  - Pruritus
  - Muscle spasms
  - Increased blood creatinine phosphokinase
  - Rash

Journavx package insert from VERTEX, revised January 2025

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Suzetrigine (Journavx™)

Pregnancy
- Insufficient data to evaluate risk for adverse maternal or fetal outcomes

Lactation
- No data on presence in human milk. Not recommended while breast feeding

Pediatric
- Safety and effectiveness has not been establihsed

Geriatric
- No data available (clinical trials did not include significant number of patients > 65 years)

Journavx package insert from VERTEX, revised January 2025

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Suzetrigine (Journavx™)

Copay Cards

- As low as $30 per month
- https://www.journavx.com/support
- Mail in rebate available

Patient Assistance

- https://journavxpap.com/

Journavx package insert from VERTEX, revised January 2025

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Honorable Mention: Neffy (epineprhine nasal spray)

Indicated to treat type 1 allergic reactions

- First and only needle-free way to administer epinephrine
- Approved in adult and pediatric patients ≥ 30 kg
- Each device contains 2 mg epinephrine
- Always carry 2 devices
- If no response after 5 minutes: administer second dose in the SAME nostril

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TOP Guidelines Expected in 2025

Organization	Topic/Guideline
ATS/IDSA	Community-Acquired Pneumonia
ATS	Pediatric Pulmonary Hypertension
ACC/AHA	Acute Coronary Syndromes
AAO-HNS	Surgical Management of Chronis Sinusitis
IDSA	Complicated Intra-Abdominal Infections (Part II)
ACC/AHA	Hypertension
GINA	Asthma

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Expanded Access

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Medication Access

Uninsured	Medicaid	Medicare	Commercial
▪ Patient Assistance Foundations –Manufacturer –3rd Party ▪ Welvista	▪ Likely requires PA ▪ May require step therapy or preferred product	▪ Often requires PA ▪ Consider deductible ▪ Potential for Patient Assistance Foundation –Manufacturer –3rd Party	▪ Often requires PA ▪ Usually requires step therapy or preferred product ▪ Consider deductible ▪ Copay/coupon cards

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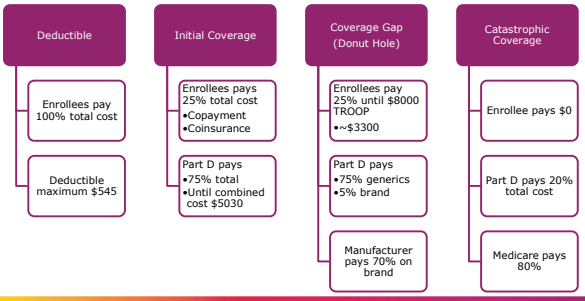
2024 Part D Benefits



https://scbluemedicare.com

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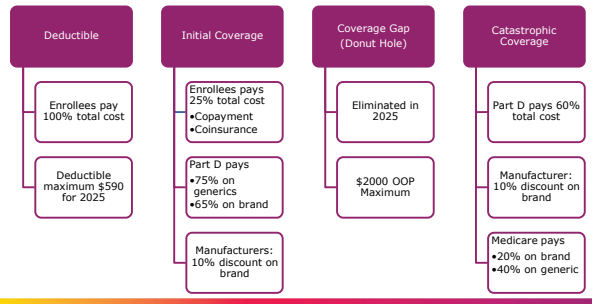
2025 Part D Benefits



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Medicare Prescription Payment Plan (MPPP)

https://ritterim.com/blog/preparing-clients-for-the-new-medicare-prescription-payment-plan-program/#pdp-ebook

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Medicare Prescription Payment Plan (MPPP)

	Jan	Feb	Mar	Apr	May	Jun
Drug Cost	$410.00	$305.00	$210.00	$210.00	$210.00	$210.00
MPPP Cost	$34.17	$61.89	$82.89	$106.23	$132.48	$162.48

	Jul	Aug	Sep	Oct	Nov	Dec
Drug Cost	$210.00	$210.00	$25.00	$0	$0	$0
MPPP Cost	$197.48	$239.48	$245.73	$245.73	$245.73	$245.73

Total Drug Cost: $2000 = Total MPPP Cost: $2000

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Medicare Prescription Payment Plan (MPPP)

Key Updates with Medicare Part D and MPPP:

- No coverage gap (donut hole) in 2025
  - Prices will not suddenly increase after deductible has been met
- MPPP must be opted into by contacting Medicare via
  - phone (1-800-633-4227)
  - website (www.medicare.gov)
- If opted into MPPP, then cost will be added to monthly premiums
  - Copay should not be paid at the pharmacy
- All Part D plans have a maximum out of pocket of $2000

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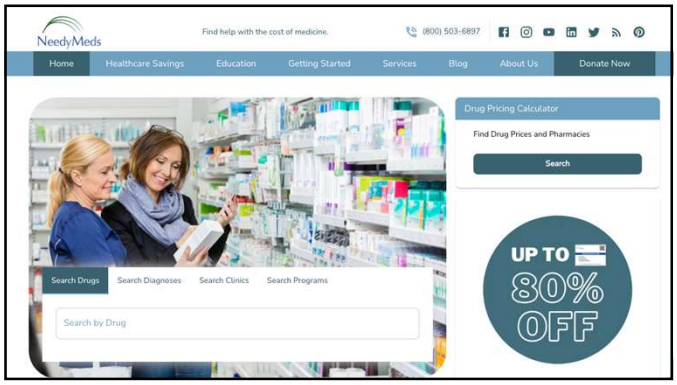

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Welvista Pharmacy (welvista.org)

Income criteria: ≤200% Federal Poverty Level

Completely Free

90-day supplies shipped directly to patient

Brand & Generic Products

Do You Qualify?

To find out if you qualify and to apply, you must be able to provide several pieces of information. Here's a quick overview:

- You must be uninsured – no Medicaid, Medicare, VA Health Benefits, etc.
- You must live in South Carolina
- You must provide proof of income for each person in your home

Learn More About Eligibility

View The Medications Available

We regularly have over 180 available medications and get new shipments every month. You may view the entire list online!

View The Medications List

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Copay Cards & Patient Assistance

Copay Cards

- Restricted to commercially insured patients
- Reduce copay with annual or monthly maximum
- If prior authorization required by insurance, will need approved

Patient Assistance

- May be available through manufacturer or third-party
- Available on basis of uninsured or under-insured status
- Income cut-offs for eligibility

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Lab to Label:
2025 New Drug Update

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Clinical Pharmacy Specialist
Prisma Health Cardiology
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